THE JOURNAL OF NEUROLOGY AND PSYCHOPATHOLOGY

Vol. XVII. JANUARY, 1937 No. 67

Original Papers

THE CEREBRAL CIRCULATION: SOME NEW POINTS IN ITS ANATOMY, PHYSIOLOGY AND PATHOLOGY *

By

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INTRODUCTION

It is not many years since the current teaching in regard to the cerebral circulation might be summed up in the anatomical doctrine that the vessels were 'end-arteries,' without anastomoses distal to the circle of Willis; the physiological doctrine that the cerebral vessels were without vasomotor supply, and changed their calibre only passively as a result of changes in the systemic blood pressure; and the pathological doctrine that thrombosis in the brain caused softening, and rupture of a vessel caused apoplexy. During the last two decades, a large number of investigators have approached the subject afresh along many different avenues, and have established a body of data which places the whole matter in an entirely new light. To review all of the work which has been done during this period would require far more than an evening's lecture, but although it is obvious that additional facts mean additional complications, certain broad principles stand out which have won general acceptance, and it is these that I should like to present here. Not only have the structure and function of the cerebral circulation a great theoretical importance, but they possess a considerable practical importance for diagnosis and treatment as well, and promise even more for the future.

* This is the tenth of a series of papers of which the expenses were defrayed in part by the Multiple Sclerosis Fund of Harvard University.

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E. Bates Block Memorial Lecture delivered at the Atlanta Medical Society, Atlanta, Georgia, January 23, 1936.

THE ANATOMY OF THE CEREBRAL CIRCULATION

The arrangement of the circle of Willis, the distribution of the larger arteries of the brain, and the course of the larger veins are, of course, matter of common knowledge and text-book record.

The main trunks of both arteries and veins run in the pia. The vessels within the parenchyma never reach the size of the larger pial vessels, and in general they tend to run in a direction perpendicular to the pia. Not only do the arteries spring from the surface, and, of course, ultimately from the circle of Willis or in the brainstem from the basilar, but the veins return to the pia and drain into the great sinuses. There are a few anastomoses with vessels of the scalp and face, but they are of little importance in maintaining nutrition. Even the vessels supplying and draining the choroid plexuses run in the tela choroidea, which is a fold of pia. There have been singularly few investigations of the finer anatomy. It has been accepted almost universally that there were no anastomoses between the cerebral arteries on the authority of Cohnheim. Cohnheim arrived at this conclusion from the results of experimental embolism, which produces areas of necrosis more rapidly in the brain than in any other organ of the body. He did not, however, make any extensive anatomical investigations, and those of the period (for example, in the hands of Duret and of Key and Retzius) gave a rather incomplete picture of the actual situation.

Perhaps the first to demonstrate clearly the anastomoses of the cerebral vessels was Fay [1] in 1925. He injected liquid mercury into one of the branches of the circle of Willis in a human brain after removal from the skull, and was able to demonstrate by X-ray that the injection mass would gravitate by way of anastomoses from one pole of the brain to the other and even across the midline. The subject was taken up in a more systematic manner by Pfeifer [2] and Cobb [3] in animals, and more recently by Pfeifer [4] in human material. By means of an injection technique, they have been able to demonstrate a rich anastomosis between capillary beds and between different systems of veins, a considerable anastomosis between neighbouring arterial systems, and even some short-circuits between arteries and veins. Pfeifer's many beautiful specimens leave no shadow of doubt that anastomoses between the various arterial systems do exist, and I have been able to confirm his findings in our own laboratory.

Not all of the details of the anatomy of the cerebral circulation need concern us here. I should, however, like to call attention to a few of the outstanding facts. In the first place, Cobb and Talbott,[4a] extending the work of Craigie, showed that from a quantitative point of view the white matter possesses a relatively sparse blood supply, while the grey matter contains almost as many millimetres of capillary per cubic millimetre as does resting skeletal muscle, though it is far behind the cardiac muscle in its vasculature. It is probable, however, that the cerebral capillaries are more constantly

open than those of most other organs. We might say that it takes far more power to propel the ship than it does to operate the rudder and signal system, but that when steam is low, the captain's bridge is supplied first.

In the second place, I may point out that each area in the brain appears to possess peculiarities of blood supply which are as distinctive as its cellular architecture. In some instances, these peculiarities appear to be of especial pathological importance. It has long since been suggested that the selective localization of diseases of the central nervous system was in part due to regional differences in blood supply (Spielmeyer,[5] Schwartz and Cohn [6]), and the intensive studies of recent years make this seem even more likely. Thus Pfeifer points out [7] that the capillary dilatation which accompanies

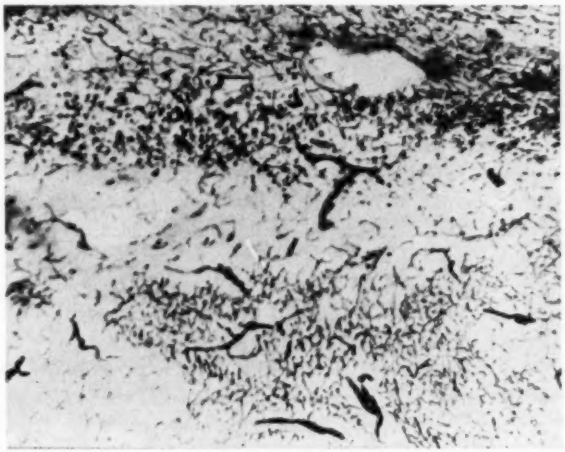

FIG. 1.—The relatively scanty blood supply of the human substantia nigra, distinguished by its large pigmented cells (above), contrasted with that of the red nucleus (below). Injected autopsy specimen, unstained, 100μ thick. Low power.

cerebral tuberculosis in the monkey spares the globus pallidus which is characteristically most severely damaged by a group of poisons including carbon monoxide, methyl alcohol and benzol. Pfeifer [4] and also Finley [8] have shown that the venous drainage of the cerebellum is peculiar, in that the white matter of the convolutions contains no large veins, while the dentate nucleus and its surroundings contain many. Finley has made a convincing attempt to correlate the localization of many acute encephalitic lesions in the latter region with the anatomical arrangement of the blood vessels. There appear to be peculiarities in the capillary supply of the substantia nigra which may explain in part its vulnerability toward epidemic encephalitis (fig. 1). This has been made the subject of special study by Finley.[9] In a similar manner, Cobb [10] has pointed out the differences in

capillary pattern between the lenticular nucleus and the cortex which may explain the localization of the lesions of paralysis agitans and carbon monoxide poisoning in the former. The list of possibilities could be extended almost indefinitely, but so far crucial investigations have been scanty. I shall return to some of the few definite practical applications of the study of vascular pattern a little further on.

NERVE-SUPPLY OF THE CEREBRAL BLOOD VESSELS

There can no longer be any doubt that the vessels of the brain are accompanied by nerves, medullated and bare. They have been demonstrated in pial vessels by Stöhr,[11] Hassin,[12] Penfield [13] and others, in parenchymal vessels by Penfield,[13] and in the choroid plexus by Clark,[14] and by Ask-Upmark and Putnam.[15] As will be seen below, there is every reason to believe that these nerves control the calibre of arterioles. It is not known whether they may also have a sensory function. Stimulation of the dural arteries and of the great sinuses in the human being produces pain (Fay,[16] Penfield [17]), and there is some evidence that stimulation of the pial vessels may produce pain reactions (Fay,[16] Levine and Wolff [18]). Certainly the choroid plexuses are insensitive, for I have applied a coagulating current to them in hydrocephalic infants under light anæsthesia on many occasions without evoking a response.

The exact connexions of the vascular nerves with the peripheral nervous system are not well known. Section of the cervical sympathetic chain produces an increase in the number of visible capillaries of the homolateral hemisphere,[19] but it is not certain that the effect is permanent. A pathway for vasodilator fibres has been described, passing from the geniculate ganglion to the carotid plexus.[20] Sensory fibres apparently enter the trigeminal, the glossopharyngeal and the vagus roots, according to an ingenious analysis by Fay.[16] Much work is still needed to elucidate this important problem, which may easily contain a clue to more efficient methods of treating the severer forms of headache, certain types of epilepsy, and even perhaps some of the structural abnormalities of the brain.

PHYSIOLOGICAL CONSIDERATIONS

No animal species could survive if its members were not provided with a mechanism for maintaining the blood supply of the brain through the ordinary vicissitudes of life. Obviously, the cerebral blood flow will be lessened if the systemic blood pressure falls, and there must exist some kind of an automatic balance between the two. Is this wholly on the part of the systemic blood pressure ?

A definite answer to this question necessarily waited upon the invention of a suitable method of investigation, which was first systematically applied by Forbes and his associates.[21] Over a series of years these investigators

have studied the pial vessels in living animals under the microscope, through an ingenious 'window' which is screwed into the burr-hole in the skull in such a way as to make a waterproof joint, thus preserving normal pressure relationships. By taking careful measurements and photographs, Forbes and his associates have shown conclusively that there is a vasomotor control of pial arterioles. They can be made to contract briskly by stimulation of the cervical sympathetic. Even more striking is their response to chemical stimuli. The presence of carbon dioxide, ether, histamine, and amyl nitrite in the blood causes a marked dilatation, while epinephrin applied locally or hypertonic solutions in the blood stream cause a contraction. Caffein causes first contraction, then dilatation.[22]

Such experiments do not necessarily answer the question of the relative importance of changes of calibre in the cerebral and in the systemic vessels respectively. Forbes himself, and with Pool and Nason,[23] has pointed out that the effect of sympathetic stimulation is far greater upon the vessels of the skin and dura than upon those of the pia. On the average a given current applied to the sympathetic in the neck caused a contraction of about 8 per cent. diameter in a pial artery, and about 80 per cent. contraction in a vessel in the skin, practically obliterating it. Schmidt [24] has shown that if epinephrin is added to a fluid injected into the common carotid of a cat, the injection is practically confined to the brain, which remains almost uninjected otherwise. Direct measurement of the rate of flow through the monkey's internal carotid under constant pressure by Finesinger and Putnam [25] showed clearly that stimulation of the sympathetic or the introduction of epinephrin caused a retardation of circulation, but that this could be compensated for by raising the perfusion pressure moderately. This experiment, and also direct observation of vessels in the choroid plexus and floor of the ventricle by Ask-Upmark and Putnam,[15] indicate that the vessels actually in the cerebral substance react to chemical and nervous stimuli less readily than those in the pia, which in turn show a much smaller range of contraction than those of the skin. Thus the administration of histamine, though causing a dilatation of cerebral vessels, decreases the flow through them, while epinephrin produces an increased flow.

To sum up the physiological data, we must certainly accept the fact that the cerebral vessels are capable of contracting, but this mechanism is probably to be regarded as an accessory, rather than the main one, for regulating the cerebral blood flow under ordinary circumstances.

THE QUESTION OF SPASM OF CEREBRAL VESSELS IN THE HUMAN BEING

Are there any clinical syndromes resulting from spasm of cerebral vessels? It has long since been suggested that some cases of epilepsy are due to local vasoconstriction of cerebral vessels. Penfield [26] has actually observed the constriction of a pial artery at the onset of a convulsion during

an operation on an epileptic patient. Some convulsant drugs are vasoconstrictors.[27]

On the other hand, Gibbs, Lennox and Gibbs [28] were unable to demonstrate any alteration in internal jugular blood flow preceding a convulsion in ten patients studied by an ingenious and apparently adequate method. It is possible that a local vascular spasm may take place without materially disturbing the total rate of cerebral blood flow. Sudden occlusion of a cortical vessel may precipitate focal convulsions, and abnormalities of vascular pattern are frequently found in the brains of patients with epilepsy. To me, an attractive hypothesis is that a cortical injury of almost any type may be followed by the formation of a new capillary plexus which may acquire an abnormal innervation. It is a matter of common experience that extensive scars of the skin may show an excessive reaction to sympathetic stimuli, and that nerves caught in scars become involved with new-formed vessels. May not the vessels in areas of granulation tissue in the brain also become more sensitive to various stimuli? The subject is in need of further investigation; meanwhile, it cannot be said that attempts at therapy which are based on the conception of the vascular origin of convulsions have led to any striking clinical results.

The cause of *migraine* has also been sought in cerebral vascular spasm. The syndrome may be closely imitated by congenital aneurysm of the circle of Willis, and by thrombosis of cerebral vessels.[29] Spasm of retinal vessels during the attacks has been described,[30] but I must confess that I have never observed it. Wolff [31] has recorded the presence of unusually large excursions of the spinal fluid when a lumbar puncture is performed during the headache produced by injection of histamine and regards them as due to excessive arterial pulsations. But the headache of migraine appears to be of a different type, and ergotamine tartrate, the most effective remedy for migraine, does not increase cerebral blood flow as much as do other drugs, e.g. adrenalin and histamine, which are therapeutically ineffective.[32] So this question also must still be left open.

Certain transient *paralyses* and other focal symptoms have also been ascribed to cerebral vascular spasm. It is a common observation that patients with arteriosclerosis especially may suddenly develop aphasia or hemiparesis, which lasts a few hours, and then as suddenly disappears. Such attacks are often harbingers of a more severe and more permanent recurrence, and there can be no doubt that one factor in their production is an impairment of the collateral circulation. It has been suggested by Ricker [33] and Riser, Mériel and Planques,[34] that the presence of an arteriosclerotic plaque may cause a mechanical stimulation and spasm of the vessel, but I know of no method of testing the hypothesis. Looking at a sclerotic vessel under the microscope, one wonders how much it could contract. The transient symptoms may also be regarded as the result of a temporary œdema resulting from a thrombus. In either case, the clinical significance of the occurrence

is the same ; the reserve capacity of the cerebral circulation has been impaired and an attempt should be made to lighten the patient's burdens, but he should be encouraged to moderate exercise.

In certain groups of cases, the existence of cerebral vascular spasm of a sufficient degree to cause focal symptoms seems extremely probable. Osler [35] pointed out that transient hemiparesis and other focal signs may accompany Raynaud's disease of the extremities. Kennedy [36] has called attention to the cerebral complications of the anaphylactic state. Occasionally cases are seen in which the presence of spasm of cerebral arteries seems probable, but the cause of the spasm is obscure. An example is the following :

> An Italian woman of 34 was admitted to the Boston City Hospital on account of nephrolithiasis. Following operation, and without obvious cause, the left leg became cyanotic and pulseless. The femoral artery was explored on the presumption that it was occluded by an embolus, but instead it was found in a state of spasm. Later the patient developed a left hemiparesis and right hemianopia, which receded and recurred several times. It was observed that the left leg became pulseless, and the patient had an asthmatic type of breathing and complained of anginoid pains with each exacerbation of the cerebral symptoms. The symptom complex was sometimes precipitated by emotional upsets, but otherwise no cause for it was found. This case will be reported in more detail by Novak.[37]

PATHOLOGICAL CONSIDERATIONS

The most striking fact about the cerebral circulation is that even relatively minor disturbances of it may lead to permanent and irreparable parenchymal damage. While a tourniquet may be applied to an extremity for fairly long periods without appreciable harm, and even cardiac muscle may recover from partial anæmia, or compensate for a scar by hypertrophy, the central nervous system possesses neither capacity to more than a minimal degree. Cannon and Burket [38] have shown that the cells of the cerebral cortex are destroyed by 10 to 13 minutes' anæmia—a fact which has long been known to obstetricians—and that the lower nuclei have only somewhat greater resistance.

If the entire blood supply to the brain is cut off, as was done by Gildea and Cobb,[39] the animal goes at once into a convulsion and is completely paralysed. If the anæmia is continued for about 10 minutes, permanent damage remains. The cells of the cortex—especially the larger ones—are destroyed. The animal may show signs of focal damage or may merely become apathetic, untidy and lacking in initiative.

The results of a generalized long-continued mild asphyxia may be entirely different. They are clearly seen in the cases of congenital heart disease studied by Bodechtel.[40] There was a widespread degeneration of myelin throughout the brain, with only mild changes in the cortical cells or axis-cylinders, followed by gliosis and a slight inflammatory reaction. This picture corresponds to that known as diffuse sclerosis which, as we shall see,

may doubtless arise in other ways also. A similar histological picture was produced experimentally in dogs by Ferraro,[41] by administration of sub-lethal doses of cyanide over a long period, which of course seriously impairs the capacity of the tissues to utilize oxygen. Similar lesions might be expected in certain types of anæmia, but they have not been reported. The degenerations in the white matter in pernicious anæmia are of another type,[42] and

FIG. 2.—Carbon monoxide poisoning. Softening of the lenticular nucleus and disseminated lesions elsewhere in the white and grey matter, all centring about thrombosed vessels.

probably due to a more specific nutritive lack. The differences between the results of a brief, intense general anæmia of the brain and those of a mild chronic asphyxia are probably explained by the fact that the grey matter has a richer blood supply, but also a greater reducing power and need for oxygen than the white matter. If no oxygen is available, the nerve-cells are destroyed at once; if there is just enough to support the grey matter, the circulation of the white matter is insufficient to support it. Possibly

under some circumstances, for example in the medulla and spinal cord, the grey matter may actually absorb the oxygen before it can reach the white, for the vessels supplying and draining the white ordinarily run through cellular areas, and both share the same capillary network.

The results of damage by certain poisons, such as carbon monoxide and methyl alcohol, are more complicated and difficult to understand. Often their most striking feature is a necrosis of the globus pallidus (fig. 2), but focal necroses in other parts of the grey matter and in the white matter [43] may occur. Not all of the changes and perhaps none of them are to be ascribed directly to general asphyxia or toxic injury, however, for the lesions may be found to contain fresh thrombi which could entirely account for them

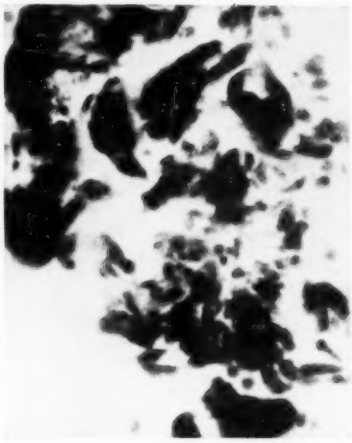

FIG. 3.—Thrombosed vein from the above case. The dark masses are fibrin, the small spheres platelets. Masson stain. Oil immersion.

(figs. 2 and 3). The problem has more than an academic interest, for various substances such as methylene blue are often administered in carbon monoxide poisoning to combat the asphyxia. It is my personal belief, based on an extended attempt to produce lesions in animals with carbon monoxide, that such medication is unwise, on the grounds that removal of the patient into the fresh air is sufficient to overcome the asphyxia at once if ever, and that any residual symptoms are the result of a parenchymal damage which the methylene blue will not affect. Artificial respiration is far more important.

The characteristic localization in the globus pallidus is doubtless to be explained by the peculiarities of its blood supply which, as we have seen, consists of a much finer network of small capillaries than is found in other areas of grey matter (figs. 4, 5), but it is uncertain whether vascular obstruction is more easily produced in this area than elsewhere, or whether it is

more destructive, or whether the region is more susceptible to general asphyxia on account of its blood supply.

The focal lesions of carbon monoxide poisoning which may be considered a typical result of a local thrombosis lead us to a more general consideration of circumscribed vascular lesions.

The most familiar and typical result of a sudden stoppage of the blood supply to an area of the brain is a focal necrosis. All of the structures in the area—nerve- and glial cells, fibres, myelin and vessels—are destroyed.

FIG. 4.—The lenticular nucleus of a human brain, injected after removal from the skull. Note the delicacy and fineness of the capillary network as compared with that of the parietal lobe (fig. 5). Section 100μ thick, lens enlargement.

If the subject survives, phagocytosis and a 'reactive inflammation' occur, and the end result is a cyst or a scar of mixed glial and fibrous tissue. If the necrotic area includes both white and grey matter, the grey matter is usually more affected than the white matter. There are certain regions in the brain, such as the internal capsule, where such necroses are particularly common, but this is all an old story, and I shall not pursue it further.

It may not be out of place, however, to say a word about the relation between thrombosis and hæmorrhage. There is good clinical and some pathological evidence that thrombosis regularly precedes extravasation of blood in arteriosclerosis and also occasionally following head injury. Just

what is the mechanism of rupture is not always certain. It has been considered secondary to a necrosis of the vessel wall (Globus and Strauss [44]) which certainly may occur, but usually only when the lumen is already filled with clot, which should prevent extravasation. In some of Alexander's cases [45] it appeared that a thrombosis in a venule—which is a common site for the formation of a thrombus—had permitted a rise in the pressure in the capillaries proximal to it sufficient to rupture them.

It is less well recognized that vascular closure may occur without causing an appreciable parenchymal damage. This was brought strikingly to my

FIG. 5.—Parietal cortex of a human brain, from the same section as that from which fig. 4 was taken. To illustrate the difference in capillary architecture.

attention a few years ago when I was studying cerebral embolism with a corn starch suspension. The starch granules are of just the right size to plug arterioles, though they pass easily through larger trunks. I was astonished to find that an appreciable quantity of starch suspension could be injected into a cat's carotid without producing parenchymal damage. In sections, the starch granules could be seen lying in the tissues without provoking any reaction.[46] This is a demonstration of the richness of the anastomoses in the cerebral circulation. It is probable that softenings only occur when a large extent of the vascular tree becomes filled with a thrombus, or when the last of the group of vessels supplying the same spot becomes closed.

There are all transitions between no permanent change and a complete

destruction of parenchyma following anoxæmia. In most instances, the injury follows a certain pattern. If a large artery becomes slowly obstructed, the changes in the area which it supplies are entirely comparable to those in the whole brain following a chronic anoxæmia, for example, of the type produced experimentally by Ferraro [41] with cyanide poisoning.

FIG. 6.—Post-vaccinal 'encephalitis.' There is engorgement of all vessels, but particularly of the veins, which are strikingly tortuous. Perivenous hæmorrhages, deposit of blood pigment, and destruction of myelin may be seen. Many of the veins contain platelet thrombi. Mallory's connective tissue stain, lens enlargement.

Among the cases which Alexander [45] studied in this laboratory was one in which a thrombosis of the basilar artery and of some of its extracerebral branches had taken place, without gross obstruction of intracerebral vessels. The result was a small area of necrosis in the pons and a large area of demyelination with less severe loss of axiscylinders. Such diffuse, incomplete lesions are more frequently seen following venous thromboses. Of course, an

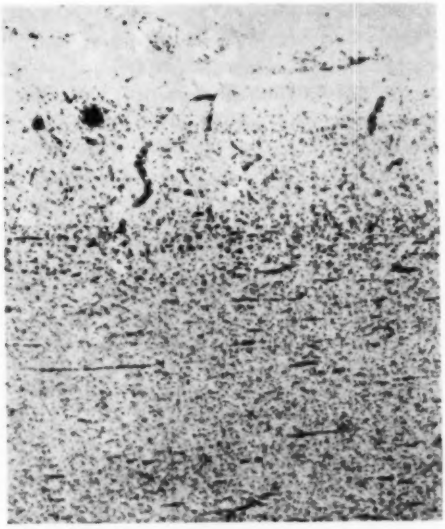

FIG. 7.—An atrophic area in the cortex of a case of general paralysis. Cresyl violet stain, low power. For comparison with fig. 8.

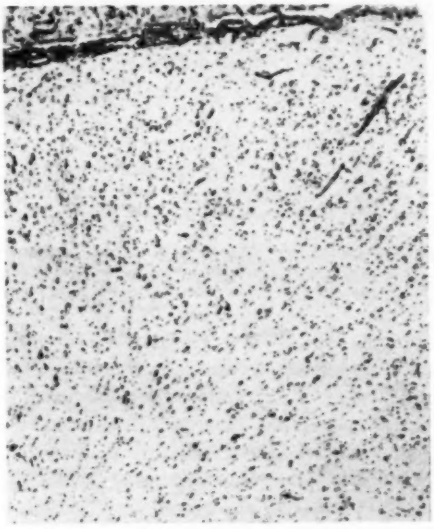

FIG. 8.—Atrophy produced in a dog's cortex by experimental capillary occlusion from the venous side. Note the similarity to the atrophy of general paralysis (fig. 7). Cresyl violet stain, low power.

extensive venous thrombosis, for example, of the longitudinal sinus and several branches, leads to a complete necrosis just as an extensive arterial closure does. But thrombosis of a small vein leads merely to a local congestion, which usually affects the white matter more than it does the more vascular grey matter, and leads principally to a loss of myelin. This can readily be demonstrated experimentally,[47] as well as in autopsy material.

Such lesions in the acute stage present all of the histological characteristics which we associate with a condition known as 'disseminated encephalomyelitis' or 'perivenous leucoencephalitis,' including the socalled 'inflamma-

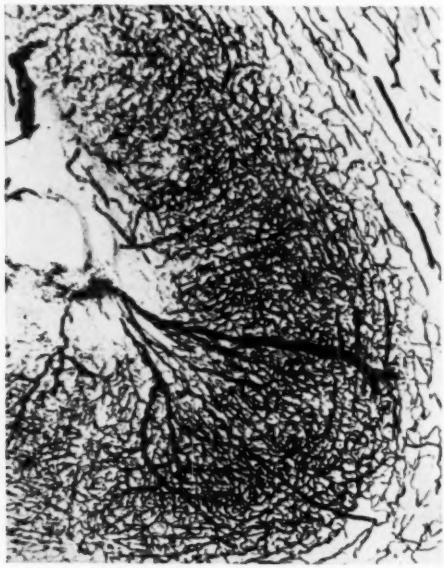

FIG. 9.—Capillaries in a normal human frontal cortex. Lepehne's stain, section 100μ thick, lens enlargement (courtesy of Dr. Colin Campbell). For comparison with fig. 10.

tory' phenomena; the post-vaccinal, post-measles, and post-German measles forms of encephalitis are the best known examples of the type (fig. 6). In the later stages, the milder injuries resulting from vascular closure closely imitate the plaques of multiple sclerosis. I have elsewhere [48] given evidence which suggests that these various diseases are produced by disseminated thromboses of small cerebral vessels, and that this in turn is the result of chemical changes in the blood plasma, rather than the direct effect of a specific infectious agent. Schilder's encephalitis periaxialis diffusa and diffuse sclerosis should probably be included in the same category.

Local lesions short of complete necrosis may also occur in the grey

matter. Those due to embolism or arteriosclerotic closure are usually small, and characterized by a local loss of, or severe damage to, nerve-cells—the socalled 'Erbleichungsherd' or faded area, since in gross the distinctive colour of the grey matter is lost and it appears to merge into the white. A common cause of sudden focal destruction of nerve-cells is syphilitic endarteritis of a cortical vessel, often accompanied clinically by focal convulsions of acute onset.

It is possible to produce small areas of 'fading' experimentally by arterial embolism. A similar, more widespread change may be brought

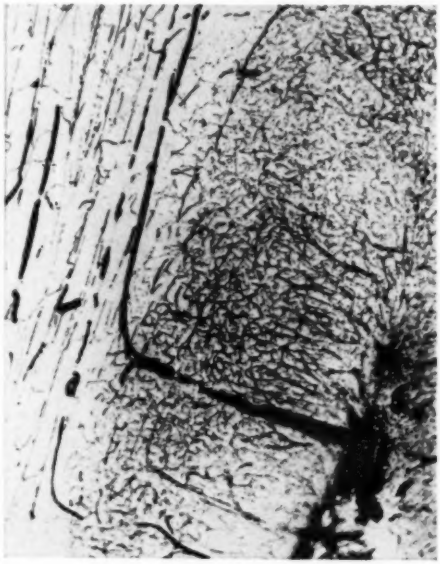

FIG. 10.—A similar area from the brain of a case of general paralysis. Notice the relative poverty and flattening of the capillary network. Lepehne's stain, section 100μ thick, lens enlargement (courtesy of Dr. Colin Campbell).

about by experimental obstruction of the capillaries from the venous side, by forcing some bland material upstream into a cortical vein.[47] As a result, nerve-cells are damaged or disappear over a wide area and there is a perivascular accumulation of phagocytic and 'inflammatory' cells, including what appear to be plasma-cells. The glia proliferates and rod-cells appear. In short, the histological picture precisely imitates that of the cortical atrophy of general paralysis (figs. 7, 8).

There may be significance in this fact. There can, of course, be no doubt that general paralysis is ultimately the result of infection with the treponema pallidum. The meningitis which is usually present is a natural

enough result of the infection, but the irreparable parenchymal damage is often seen in areas in which inflammatory phenomena are mild or absent. It has seemed to Dr. H. Houston Merritt and me [49] that possibly the disappearance of nerve-cells might be due to obstruction of capillaries by a syphilitic endarteritis. It has long been known that the capillaries in cases of general paralysis are often closed by endothelial hypertrophy, and we have been able to show that the number of capillaries containing blood is greatly diminished in atrophic areas in the cortex (figs. 9, 10). Curiously enough, the anterior horn cell destruction of syphilitic progressive muscular atrophy

FIG. 11.—Section of the brain of a case of multiple sclerosis, injected after removal from the skull. Dilated, tortuous engorged vessels in a plaque bordering on the ventricle. Section 100μ thick, unstained, lens enlargement.

has been explained long since as the result of hypertrophy of capillary endothelium (and this we have also observed), but a similar explanation of the cortical changes has not been advanced.

This conception may have a practical application. The treatment of general paralysis with fever is one of the great therapeutic advances of modern neurology. Fever is an efficient agent in dilating cerebral capillaries. It is possible that the success of the treatment is in part due to the hyperæmia of the cortex and that even more effective agents may be found by search.

I have so far mentioned only the results of vascular obstruction. The circumstances under which cerebral vessels dilate and multiply is an almost

unexplored field. A brilliant beginning has been made by Pfeifer,[7] who has demonstrated an apparently specific type of capillary dilatation in tuberculous monkeys. The plaques of multiple sclerosis often exhibit an extraordinary increase of vessels, and sometimes characteristic vascular patterns (fig. 11). Abnormal proliferation of cortical vessels almost angiomatous in character is occasionally observed following head injuries. But all these matters still contain obscure points.

CONCLUSIONS

In the present survey I have attempted to call attention to some of the directions along which the newer information about the cerebral circulation has aided in our understanding of diseases of the nervous system. Some of the interpretations which I have suggested still await confirmation—for example, the hypotheses concerning multiple sclerosis, encephalitis and general paralysis. But whether they are confirmed or not, I have not the slightest doubt that there are more to come, if we but look for them. If syphilitic progressive muscular atrophy is due to capillary closure, so may the nonsyphilitic form be also, not to mention acute poliomyelitis. The selective localization of the lesions of paralysis agitans in the corpus striatum, and of the lesions of tabes in the dorsal columns and the pupillary reflex centres are only a few of the problems which urgently deserve investigation. It is perhaps not too much to say that aside from congenital anomalies and the effects of tumours and suppurative processes, there are few pathological processes in the central nervous system which are not directly or indirectly the result of circulatory disturbances. I hesitate even to speculate on the possibilities in the field of mental disease.

SUMMARY

1. A survey of recent investigations of the anatomy, physiology and pathology of the cerebral circulation is presented.

2. It has been conclusively demonstrated by various investigators that the cerebral arteries are not end-arteries but possess a rich system of anastomoses. The vulnerability of the brain toward vascular disturbances is due rather to the sensitiveness of the parenchyma than to deficiency in blood supply.

3. Different regions in the brain are characterized by marked differences in pattern of blood supply. Some of the local peculiarities may be of significance in the localization of disease-processes.

4. The cerebral vessels bear nerves and are under vasomotor control by the sympathetic. The vasomotor activity of the arterioles of the brain is much less than that of those elsewhere, so that passive changes in the cerebral circulation outweigh active ones, at least under ordinary conditions.

5. The cerebral vessels react much more strongly to chemical stimuli than to nervous impulses. Carbon dioxide is a particularly active vasodilator.

6. While it is probable that spasm of cerebral vessels may cause symptoms, cases in which such an explanation appears likely are rare. The rôle of vasospasm in epilepsy and migraine is doubtful.

7. In addition to the familiar cysts of softening caused by vascular obstruction, milder types of injury may occur.

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AN INVESTIGATION OF THE ABSORPTION OF ULTRAVIOLET LIGHT BY CEREBROSPINAL FLUID IN VARIOUS DISEASE STATES

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INTRODUCTION

The examination of cerebrospinal fluid in various diseased states has become a matter of routine investigation and at times yields information of great value in particular cases—for instance, the presence of a cellular content of over 3 per c.mm. leads to a suspicion of some infective process involving the central nervous system, and the preponderance of a mononuclear type of cell suggests the probability of such infection being of a granulomatous nature, syphilis or tuberculosis. Further, an increase in the protein content of the fluid is indicative of chronic infection, while reduction in the amount of sodium chloride present below 0·6 per cent. is almost pathognomonic of tuberculous meningitis.

Of the more recent tests used in the examination of cerebrospinal fluid the precipitation of gold from a colloidal suspension of gold chloride is of peculiar interest. It appears to be an extremely sensitive test and to possess a definite diagnostic value. It is not necessary to refer in detail to this test; suffice it to say that it appears to depend on the upset of the balance of electric charges on the colloid particles in the gold solution with consequent precipitation of metallic gold. Lange's work at first seemed to suggest that in this method was to be found a specific test for neurosyphilis, since the highly albuminous fluids of general paralysis and tabes caused precipitation of gold in a manner which could be expressed as a simple curve. Other workers confirmed Lange's observations, but as the test became more widely recognized it was soon found that cerebrospinal fluids from cases other than neurosyphilis caused a similar precipitation, notably disseminated sclerosis. The test lost its specificity as a touchstone for neurosyphilis, but none the less the curves obtained are so characteristic that in association with other tests it is possible to say with considerable certainty whether a particular type of curve is caused by a fluid from a case of neurosyphilis or of disseminated sclerosis.

PERSONAL INVESTIGATIONS

It was the consideration of this type of reaction, depending as it does on some physical characteristic of the fluid—either the state of the colloid

contents or the electrolytes—that led me to speculate on the chances of finding some physical method of examination of cerebrospinal fluid whereby its varying constitution might be evidenced, and, after trying one or two methods, the effect of absorption of ultraviolet waves seemed to offer the best likelihood of success.

Early in 1927, therefore, I began a series of observations on the absorption of the ultraviolet waves, using a very primitive layout; the results, though purely qualitative, appeared to me to be sufficiently definite to warrant a more serious investigation. In consequence, I purchased from Messrs. Adam Hilger one of their new photometers, and during the last two or three years as time and opportunity have offered I have continued to make observations on the cerebrospinal fluid, the results of which are set out below.

The earlier observations made with a small spectrograph and a home-made optical bench, arc, and quartz-cell holder, etc., were put together in two short papers which appeared in this JOURNAL in October, 1929, and December, 1930.

At this time, so far as I could ascertain, there was no literature on the subject, though from a private source I heard that Campbell Smith had been observing the absorption of ultraviolet waves. I went to see him and he very kindly showed me some of his curves which dealt with spectroscopy of filtered blood serum.

Since that time one or two continental observers have made observations on these lines and their results will be referred to later in this paper.

In my early observations I had no means of calibrating my results, which were only expressible in terms of the wavelength at which absorption began; but the appearance of the absorption in cases of tuberculous meningitis was so striking that I felt justified in concluding that tuberculous fluids might be diagnosed from these spectroscopic tests. They were almost constant, but later I found one or two cases in which absorption was not so complete, so I was compelled to modify my early view, and consider that only in the later stages of the disease did such complete absorption occur. Even in the first few days of the disease, however, absorption commences earlier in the scale than in any other condition I have examined.

The only other fluid which appeared sufficiently characteristic to be easily recognized was that from cases of general paralysis of the insane, and here again the amount of absorption seemed to depend on the length of time the disease had been present.

While it was clear that such changes could not be diagnostic of any definite clinical picture and that they represented varying states of the cerebrospinal fluid, some of them might be sufficiently constant as to be suggestive of clinicopathological events. For instance, I felt that early in tuberculous meningitis absorption might be found somewhere about $\lambda 2397$; but with a further area of absorption between $\lambda 3051$ and $\lambda 2764$, later in the

course of the case, the lines seen in the spectrogram between λ2764 and λ2397 tended to disappear, while in other forms of meningitis in which recovery took place the absorbed lines between λ3051 and λ2764 tended to reappear.

This was one of the conclusions at which I arrived in 1928, namely that in meningitic conditions the cerebrospinal fluid gave a varying spectrogram, but one which could be recognized and perhaps serve as some help in prognosis. ' It is, of course, perfectly clear that such changes as I am describing in one tissue, cerebrospinal fluid, cannot carry a diagnostic label ; our labels are too gross for such minuteness. For instance, the label " general paralysis " conveys to our minds a more or less definite clinical picture, but the picture is really a moving one inasmuch as we envisage a series of events occurring in time, whereas an examination such as we are making can only show the results of certain metabolic accidents at a given moment, and such results as I have obtained must vary at different stages within the range of one disease-process. It is manifestly absurd to think, for instance, that every case of general paralysis must give the so-called paretic gold curve in Lange's test since the factors on which this test depend are probably only progressively developed. The results I have obtained spectrographically, if they have any value at all, can only suggest that certain tendencies are at work and can never have the same evidential value for a given instant as, say, the X-ray picture of a fractured bone.' [1]

It appeared to me from these early observations that such a method of investigating cerebrospinal fluid was worth more extended trials, for I could not but feel that there must be some difference in constitutions of cerebrospinal fluid in varying bodily conditions ' when one looks at the perfectly clear fluid from a case of tuberculous meningitis and an equally clear fluid from a case of tabes or general paralysis and in both finds a pleocytosis, an increased protein content, an identical chloride content, yet with very different spectrograms. The conclusion seems legitimate either that our means of chemical investigation are too gross to detect the minute differences in composition on which the spectrograms are dependent or, what is more likely, these differences depend on factors other than chemical.' [2]

METHODS

The principle of ultraviolet spectrophotometry consists of photographing two spectra one immediately below the other so that any absorbed line in the one spectrum may be compared with a similar line in the other. One of these spectra is that produced by light which is passed through the solution to be analysed, the other through a solvent such as distilled water. The source of light, e.g. the spark from an induced current sparking between electrodes of tungsten, copper, iron or other metal, gives one of the well-known ' line spectra,' and such spectra are photographically recorded and

the absorption of any of these lines is shown by its absence from the spectrum.

In spectrographic observations great use is made of a factor known as the 'extinction coefficient,' the value of which has been arrived at as follows. According to Lambert's law 'the proportion of light absorbed by a substance is independent of the intensity of the incident light,' just as a sponge can only absorb a certain amount of water irrespective of the volume or the velocity with which the water impinges on the sponge.

If J_0 be the intensity of light entering a medium and J the intensity after passing through a length of d centimetres, and if $1/a$ be that length of path, the passage through which reduces the light intensity to 1/10th, then

$$J = J_0 \cdot 10^{-ad} \text{ or } \frac{J_0}{J} = 10^{ad}$$

where a—a constant depending on the medium—is called the extinction coefficient.

This is the definition of the extinction coefficient given by Bunsen and Roscoe, and from the formula it will be seen that it is the reciprocal of the thickness of the medium which is necessary to reduce the light to 1/10 of its incident value

$$\left(a = \frac{1}{d} \log \frac{J_0}{J}\right).$$

A further term is useful, namely the 'density.' If J and J_0 have the significance given above, we may write $J = J_0 10^{-D}$, D being called the 'density.'

$$J = J_0 10^{-D}, \quad J = \frac{J_0}{10^D}, \quad D = \log \frac{J_0}{J}.$$

Therefore $D = ad$; that is, the density is the product of the extinction coefficient and the depth of the medium (in centimetres).

It is necessary to define these terms, since unfortunately they are used occasionally with other meanings, the meanings here assigned being those given by Bunsen and Roscoe [3] to the extinction coefficient and by Hurter and Driffield [4] to density.

The method of recording the absorption in these experiments is the one usually employed in this country, and consists in determining the points in the spectrum at which absorption occurs and expressing on a graph these points in terms of density and wavelength, using the former as ordinates and the latter as abscissæ.

The practical application of these theoretical considerations has proved of great use in identifying substances in solution, and although no clinical use has been made of them so far, I consider the method may eventually be found to have some importance, particularly in medicolegal work, where the spectrophotometric examination of body fluids might disclose the presence of soluble poisons.

TECHNIQUE

The actual observations are not difficult once the apparatus has been set up, though admittedly the apparatus is amongst the most delicate in use and requires some skill in adjusting, but once adjusted, observations can be made a simple routine procedure. Roughly speaking, the technique is as follows. Light is passed through the medium under examination as well as through an indifferent medium, and the resulting beams, which are parallel, are analysed by quartz prisms. The resulting spectra are received on photographic plates. Various methods have been adopted for controlling the results, but whatever method is employed the result is the same—two spectral bands, one of which is produced by light passing through the medium to be analysed, the other through the indifferent medium, are received on a

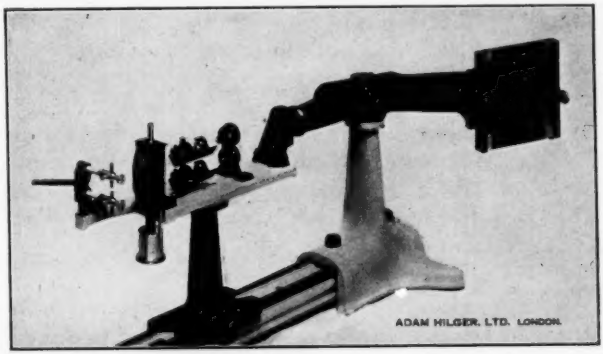

FIG. 1.*

photographic plate. The amount of light through the first is fixed, while that through the latter is variable.

When the resulting photographs of the spectral bands are examined it is clear that the photographic blackening of each line depends on the amount of light reaching the plate at that point, and if the light passing through the medium is absorbed this photographic blackening will be diminished. In two spectra juxtaposed, if it be found that two lines are of equal blackness it is proof that similar amounts of light have passed through the medium under examination and the control medium.

If any solution of electrolytes is used for analysis and distilled water for the control, the resulting spectra will show a certain amount of ' selective ' absorption, i.e. lines will be diminished in blackness in the spectrum of the light passing through the solution of the electrolytes. The corresponding lines in the spectrum of the light passing through the distilled water will be

* This is a later model than the one used in the experiments.

much darker. The various forms of apparatus are designed so that this latter beam may be so reduced in intensity that the diminished blackening produced by the absorption may be matched by reduction of light passing through the distilled water. As has been said before, when any two lines are of equal blackness it is because the amount of light falling on the photographic plate is the same in both cases; in the one case reduction is caused by absorption, in the other by reduction of light intensity. One can therefore measure the absorption by the diminution in light intensity, and thus absorption can be expressed in terms of intensity of light so measured.

The photometric method I have used in my observations is one in which this relationship is of the simplest.

The apparatus, the Spekker photometer, is seen in fig. 1.

It consists of a pair of electrodes for the spark, the light from which is passed through reflecting prisms whereby the single beam is split into two,

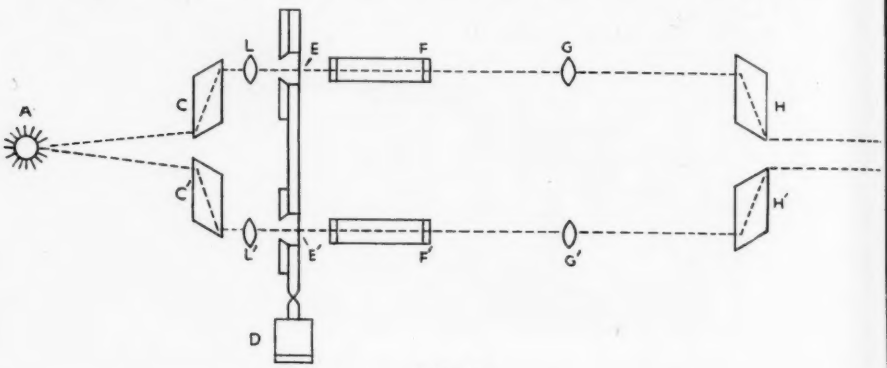

FIG. 1A.

one of which passes through the medium under examination, the other through the control medium, after which the two beams are again brought close together and directed, still parallel, into the spectrograph.

Light emanating from source A enters the quartz reflecting prism C and after undergoing a further reflection is rendered parallel by the lens L. This parallel beam of light, after traversing the medium F of which the absorbent constants are required, falls on the lens G, which focusses the light, after being reflected by the prism H, on to the slit of the spectrograph, forming there an image of one-half of the light source. A similar cone of light falls on the prism C′, is rendered parallel by L′, and after passing through the control medium F′ is focussed by the lens G′, forming an image of the other half of the source of light on the slit of the spectrograph after reflection by the prism H′.

Immediately in front of the lenses L and L′ are placed two rectangular apertures E and E′, controlling the amount of light passing through the

photometer. The aperture E in the upper path is fixed in area while the lower aperture E′ can be varied at will to give any area of opening. This adjustment is achieved by turning the drum D, which by means of an accurate screw alters the position of one of the sides of this variable aperture.

Thus the spectrograph is illuminated by two beams of light of the same origin, the intensity of one being varied by the absorbing medium under test, while the intensity of the other beam is controlled by the opening of the variable aperture. In any photograph of a spectrum (spectrogram) taken under the above conditions, the points at which the lines are of equal blackening indicate that the light passing through the material under test is equal to that which has passed through the variable aperture.

When no absorbing medium is present the spectra are of equal intensity only when the areas of the fixed and variable apertures are the same, the ratios of the respective areas being a measure of the ratios of the intensities of the two beams of light. It can easily be shown that the intensities of the two beams are proportional to the respective areas of the fixed and variable apertures.

Let J_o be the intensity of the light entering the absorbing medium and J the intensity after transmission through the medium. Then since the areas of the apertures are proportional to the light transmitted and since also at the points where there is equal blackening of the lines the area of the variable aperture has been adjusted to make the intensity of the control beam equal to that of the light after passing through the medium, the ratio $\frac{J_o}{J}$ may be represented by the expression

$$\frac{J_o}{J} = \frac{\text{area of fixed aperture}}{\text{area of variable aperture}}.$$

The drum D which controls the variable aperture has on it an engraved scale to read $\log \frac{J_o}{J}$, which logarithm, as has been mentioned above, is referred to as the density.

By taking a series of photographs with the drum set to different density values and then on the negative searching for the points of equal blackening of the lines in the two spectra, one is able to obtain a number of values of $\frac{J_o}{J}$ for a wide range of wavelengths and from the values so obtained to construct a graph connecting the density $\left(\log \frac{J_o}{J}\right)$ with the wavelength.

It will be seen from the above considerations that in order to obtain an absorption curve of cerebrospinal fluid all that is necessary, using the Spekker photometer, is to take a series of bipartite spectra on one plate with various density readings and then plot out the points at which the lines are of equal blackness.

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The rest of my apparatus consisted of an old 32-inch X-ray induction coil with a plate condenser of 0·005 microfarad capacity in parallel with the spark, the electrodes being of tungsten steel. The whole was energized by a direct current of 60 volts interrupted by a turbine motor break working direct from the A.C. mains (250 volts). The spectrograph was fitted directly to the photometer.

The exposure depends on the source of light. The best results are obtained by making it of constant actinic value by increasing the time according to the expression $E = K$ antilog D, where K is a constant depending on the source of light and D is the density.

By trial and error I found 3 seconds to be the best value for K, so that my exposure table for a single observation was as follows :—

Density	Antilog	Exposure calculated	Exposure used
0·0	1·0	3·0	3
0·1	1·26	3·78	4
0·2	1·58	4·74	5
0·3	2·0	6·0	6
0·4	2·51	7·53	8
0·5	3·16	9·48	10
0·6	3·98	11·94	12
0·7	5·01	15·03	15
0·8	6·31	18·9	20
0·9	7·98	23·94	25
1·0	10·0	30·0	30
1·1	12·59	37·77	35
1·2	15·85	47·65	45
1·3	19·95	59·85	55
1·4	25·1	75·3	75
1·5	31·6	94·8	95
1·6	39·8	119·4	120
1·7	50·1	150·3	150
1·8	63·1	189·3	190
1·9	79·8	239·4	240
2·0	100·0	300·0	300

Ilford special rapid plates were used throughout and were developed by time and temperature method.

After a negative is finished, the next step is to ' spot ' the points where the two lines in the adjoining spectra are of the same blackness. This is done by placing the negative on a viewing-box suitably illuminated with a face of opal glass, and with a fine pen marking the points on the negative with Indian ink.

When all the spectra on one negative have been so ' spotted ' (usually 15 or 16 exposures on one plate) the positions of these ink dots can be read off on a wavelength scale. From each negative at the end of this process

of spotting a table of figures is obtained composed of the wavelengths of the absorbed lines at a particular density, and with these two values a graph is made in each case.

ABSORPTION CURVE OF NORMAL CEREBROSPINAL FLUID

It was first essential to examine a specimen of normal cerebrospinal fluid, and having acquired a constant technique I made a number of observa-

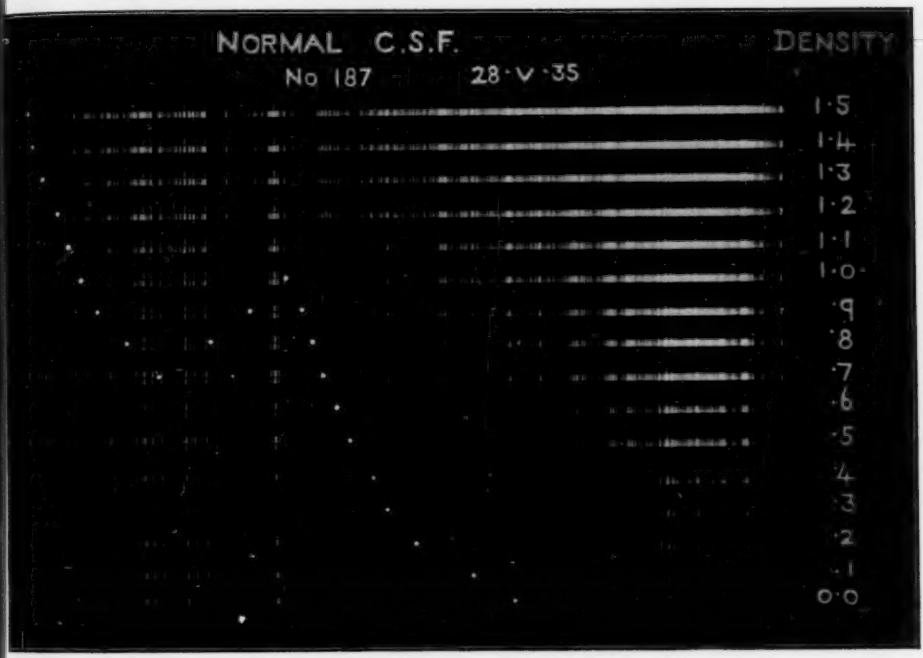

FIG. 2.

tions on normal fluids obtained from volunteers from the local Unemployment Exchange. Fig. 2 is the print of an absorption spectrogram given by normal fluid.

The 'spots' are placed on contiguous lines of similar photographic density and for the purpose of reproduction have been made unnecessarily big. Four such negatives have been used in preparing the composite graph shown in fig. 3, and it will be seen that all show absorption of almost identical kind, the variations in the graph being relatively slight.

From a study of such negatives and graphs it is clear that there is complete absorption of all waves shorter than those of $\lambda 2380$, while waves

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of a length of λ2630 are only slightly absorbed; more absorption is seen in the neighbourhood of wavelength λ2650 and λ2800 and so on. Thus, examination of a spectrogram of normal cerebrospinal fluid is found to give evidence of some selective absorption between wavelength λ2380 and λ3200.

This selective absorption is demonstrated in the graph in fig. 3, where it will be noticed that the curve is broken by a 'hump' in the middle of its course. The position of this hump with its subsequent depression and following rise is the characteristic feature of the 'absorption curve' of

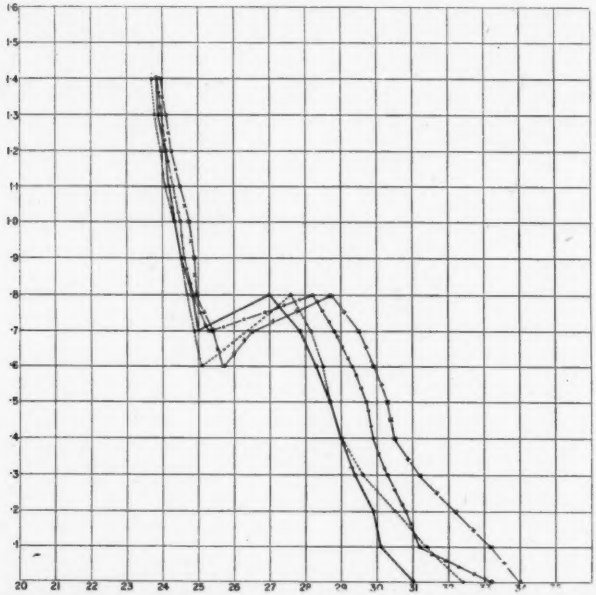

FIG. 3.—Normal cerebrospinal fluids. Composite graph from four negatives showing normal limits of variation in absorption of ultraviolet waves. Fluid obtained from four healthy persons.

cerebrospinal fluid, and, as will be seen presently, the striking differences between normal fluids and those from cases suffering from a variety of different diseased states are generally found in a particular region of the scale between λ3250 and λ2380.

PATHOLOGICAL ABSORPTION CURVES

Having determined what appeared to be the normal absorption curve of cerebrospinal fluid, I proceeded to investigate specimens from cases in which it was being examined in the laboratory in the course of routine clinical work. My first 50 or 60 cases were unselected. I received from various sources all kinds of cerebrospinal fluids, from cases of suspected cerebral tumour, myelitis, meningitis, chorea, syphilis of the central nervous system,

etc., and I would here like to thank those of my colleagues, both at my own hospital and others in the city, who were kind enough to send me material for my investigation.

A study of the absorption of ultraviolet waves in this first series of 50 cases made it clear that one or two tentative conclusions could be drawn.

1. Cases of tuberculous meningitis gave rise to a characteristic change in the curve, as did also
2. Cases of general paralysis of the insane, but here the change was not so striking.
3. During the course of a disease the curve tended to become steeper if progress was towards fatality.

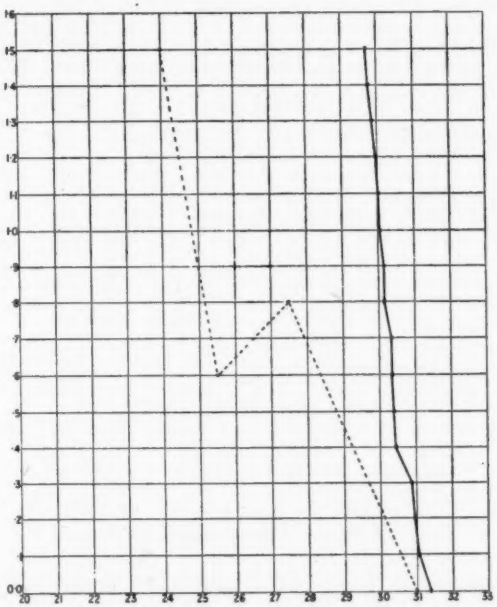

FIG. 4.—Tuberculous meningitis, late stage.

These observations tended to confirm my previous conclusions in the two papers mentioned above.

When the terms tuberculous meningitis or general paralysis are used, it must of course be understood that such can only be rough clinical labels, and an examination such as the one under discussion can only refer to a particular biochemical state at a particular time, since during the progress of a diseased condition such biochemical states must vary. It is surprising to find however that the biochemistry of the cerebrospinal fluid does remain remarkably constant.

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Fig. 4 is a print from a case of (clinical) tuberculous meningitis verified at autopsy. It will be noted that there is a striking total absorption producing an almost vertical graph (within the limits of my observational technique), though there is at times in similar cases a suggestion of a hump much higher in the graph, as is also seen in cases of general paralysis at times.

In fig. 5 a few lines appear between λ2650 and λ2500, but only when the coefficient of extinction is high (1·3), and I have little doubt that even this part of the spectrogram would be completely absorbed in a few days (in

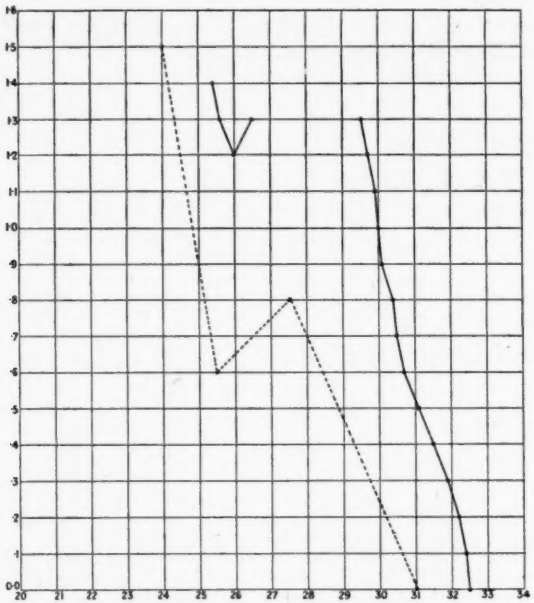

FIG. 5.—Tuberculous meningitis, early stage.

those cases where it is seen), but usually death supervenes and prevents continued observations.

That this is so is seen in fig. 4, which shows the hump, present in fig. 5, to have completely disappeared. These two graphs are from the same case, fig. 5 being the earlier state and fig. 4 that of a week later.

This persistence of a few lines seems to occur in this situation early in the disease and a similar persistence is found in many cases of general paralysis —as will be noted later. On the whole however the characteristic absorption by cerebrospinal fluid from cases of tuberculous meningitis is that seen in fig. 4. A large number of specimens of fluid from cases of tuberculous meningitis has been examined and the absorption curve is quite constant for any period of the illness and might, I think, be admitted in a doubtful

case as additional evidence should the question of diagnosis or prognosis be urgent; it appears to be of about the same evidential value as the chloride content, which tends to become lower the more established the disease. This is seen in figs. 4 and 5 from a case in which the chloride content was at first (fig. 5) found to be 0·7 per cent. and a week later was reduced to 0·6 per cent. (fig. 4).

Turning next to the fluids from cases of general paralysis, a similar constancy of curve was obtained, though, as mentioned before, it is not so

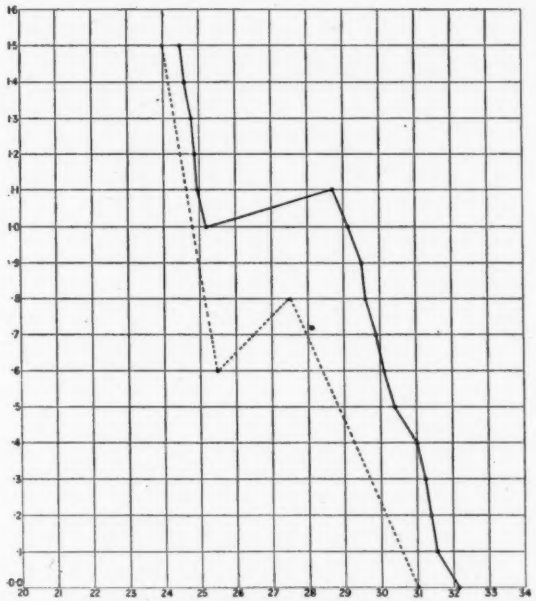

FIG. 6.—General paralysis, early stage.

striking as in cases of tuberculous meningitis. The total absorption is not so complete, beginning at λ3200 and becoming less marked as the higher densities are reached, producing a curve less steep than that in the tuberculous cases. The hump too is more frequently seen, though it is shifted towards the top of the graph and in advanced cases disappears altogether, while the total absorption also increases—that is to say, the curve is shifted as a whole towards the region of the long waves.

This last feature of shifting towards the long wave end of the spectrum has been noted by Jacobi and Winkler.[5]

Fig. 6 is the curve of absorption given by cerebrospinal fluid from a case of general paralysis. A large number of such fluids has been examined. A study of these curves brings out one or two points of interest. First, the

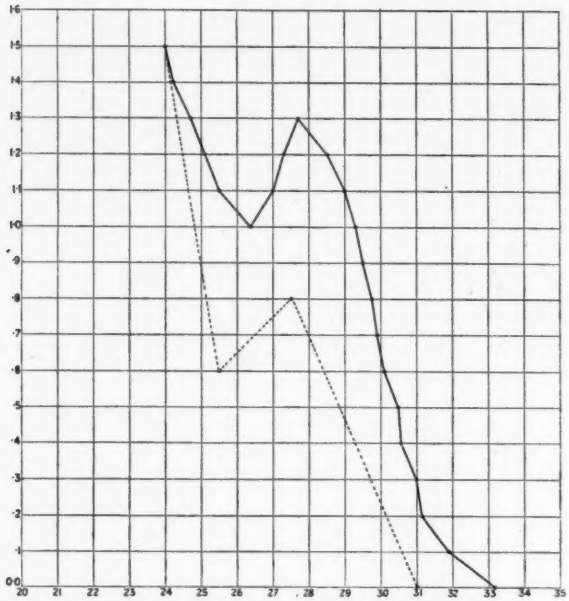

FIG. 7.—General paralysis, later stage than fig. 6.

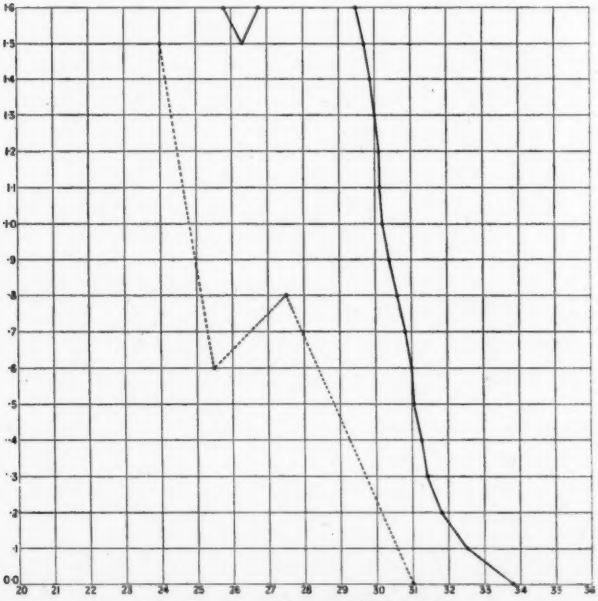

FIG. 8.—General paralysis, late stage.

type of curve varies with the stage of the disease, as one would expect; in the early stages being of the same general form as that of normal cerebrospinal fluid except that the first part of the rise is shifted a little to the right and the hump appears a little higher (fig. 6), and then showing more and more departure from this type as the disease progresses.

Fig. 7 is a curve from a case of general paralysis of longer standing, and here the hump is seen to be moving still higher in the graph, though still a

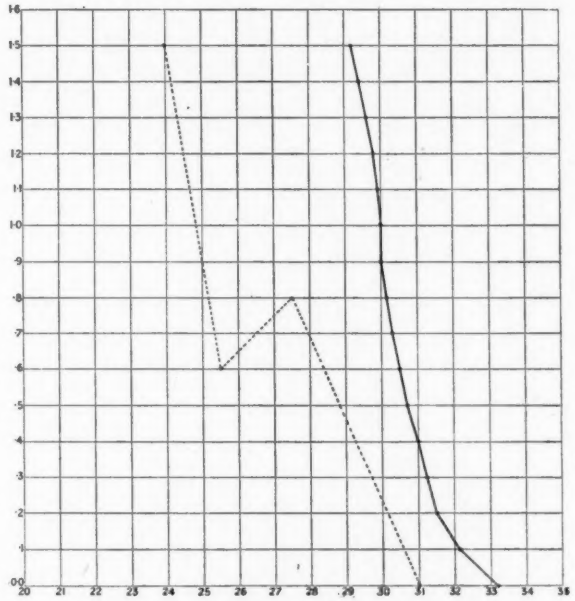

FIG. 9.—General paralysis, late stage.

complete hump; in fig. 8 the hump has moved so high that it is open at the top and has practically disappeared.

In cases of even longer standing, such as the one from which the curve shown in fig. 9 was obtained, the hump has gone completely and the absorption curve is merely a steeply sloping line, i.e. there is total absorption beyond a wavelength of $\lambda 2900$—being almost identical with the type of curve found in tuberculous meningitis.

The treatment of general paralysis by malaria has a marked influence on the curve, as can be seen in fig. 10.

This case was one of long standing and appears to have become more or less stabilized, no progress having occurred for some years. The patient was infected with malaria as long ago as 1929, and beyond a slight increase of

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globulin in the cerebrospinal fluid this is now almost normal. It will be seen that the absorption has returned towards that found in the early cases, i.e. approximating to the absorption in normal fluid. Jacobi and Winkler [5] also noted a tendency in the fluid of subjects treated by malaria injections to return towards the normal curve.

The fluid from both groups of cases, tuberculous meningitis and general paralysis, appears to give the same type of absorption curve in the fully developed disease; the differences are probably due to the short time in which meningitis runs its fatal course compared with the long course of

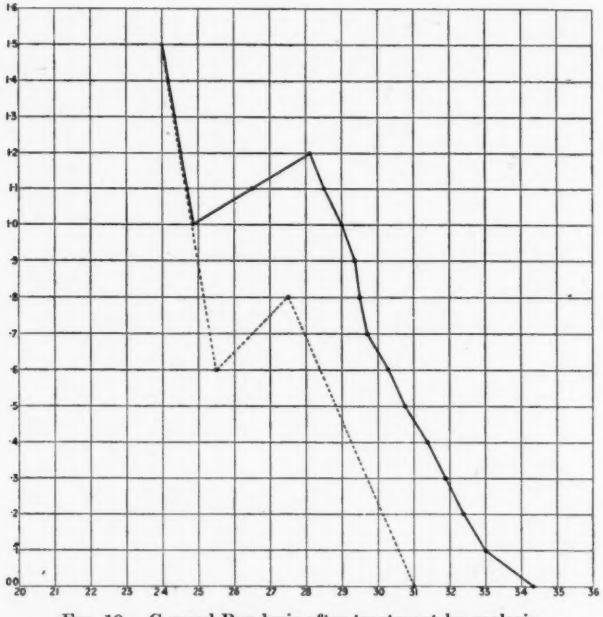

FIG. 10.—General Paralysis after treatment by malaria.

general paralysis and also to the complete absence of any change brought about by treatment in the former, whereas the effect of treatment, and possibly in some cases natural healing processes, tend to alter the appearances of the curve in the latter.

Both these clinical conditions are associated with a pleocytosis, and it seemed desirable to ascertain whether this pleocytosis per se exercised any influence on the absorption curve.

This was done by selecting a fairly early case of general paralysis in which pleocytosis was marked and plotting the curve, and then centrifuging the fluid and again plotting the curve. Fig. 11 shows these two observations on one graph, and it will be readily seen that the cell content of the fluid

has no influence on the curve, which is in accordance with my previous conclusions.[6]

I had not expected to find that such pleocytosis would produce alteration in absorption for two reasons, firstly because absorption is not influenced by suspended matter unless the latter is in such concentration as to bring about almost complete dispersion of light; and secondly because I had

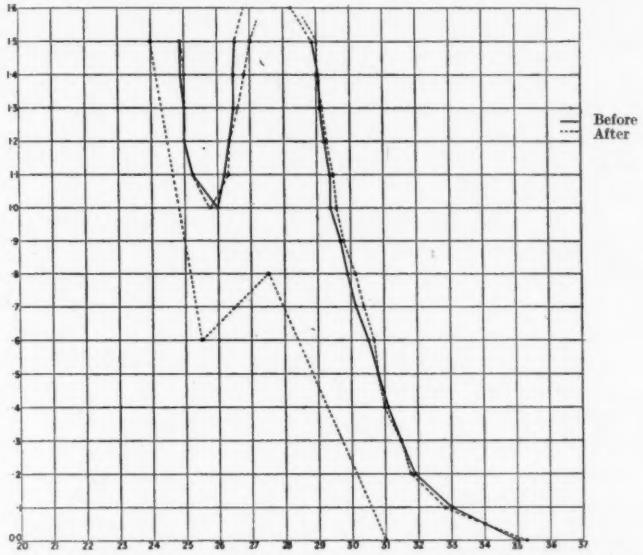

FIG. 11.—Absorption of ultraviolet rays by cerebrospinal fluid before and after centrifuging. Shows that cells have no effect on absorption.

examined a sufficient number of fluids to feel quite sure that there existed no positive correlation between cell content and absorption.

OBSERVATIONS ON DIALYSED CEREBROSPINAL FLUID

The examination of a large number of absorption spectra has led to the conclusion that, in disease, changes in the absorption curve show themselves in two ways: (1) a general shift of the absorbed areas to the long wave end of the spectrum; and (2) the disappearance of the characteristic hump seen in normal fluid.

This hump is indicative of selective absorption and in a normal curve means that there is a wide band of absorption between $\lambda 2600$ and $\lambda 3200$, then absorption ceases between $\lambda 2600$ and $\lambda 2400$ when again rays are absorbed. Were it possible to extend the observations it is likely that similar bands would be found farther along the electromagnetic scale. Repeated observations of over 200 fluids make it clear that the absorption

between λ2600 and λ3200 is a biochemical factor of normal fluid and any alteration in its position is pathological.

Since the presence of a large number of cells exerts no influence on the absorption curve, it appeared essential to try and eliminate the other possible factors that might influence it. Cerebrospinal fluid consists essentially of a dilute blood-plasma and contains normally small amounts of salts and proteins, so that separation of these two groups of constituents was the next step.

The separation of salts was attempted first, and here a considerable amount of difficulty was encountered, owing to the fact that only small amounts of fluid are ever available and that the fluid very quickly becomes cloudy. Unless all the apparatus is kept sterile the time required for dialysis to occur (usually 24 to 36 hours) is sufficient to allow contamination by organisms, with the production of turbidity and completely misleading absorption spectra.

The separation of these electrolytes was carried out by dialysis through a collodion membrane at ordinary temperatures and atmospheric pressure so far as the surrounding medium (distilled water) was concerned, the membrane being made in the form of a small bag. It was found that a 5 per cent. collodion in ether and alcohol gave a membrane sufficiently strong to withstand the osmotic pressure and yet tough enough to be handled with care.

The cerebrospinal fluid is put into the dialysing bag with a sterile 5 c.cm. Wright's pipette, the open end of the tube being closed with a tight-fitting rubber bung. This bung must have a small tube through it (I used a wide-bored needle) to allow of escape of air when being forced into the tube, otherwise the collodion bag will burst. This air-vent is easily closed by a small rubber tube which is bent on itself and clipped with a screw clamp.

The complete separation of the electrolytes was assumed when all chlorides were gone, and this was ascertained by taking a drop of cerebrospinal fluid in a sterile pipette of fine bore, and dropping it on to a microscope slide whereon was a drop of 20 per cent. silver nitrate solution. If the slide is held above a black card and looked at from above, the light falling on it at an angle, the minutest trace of a precipitate is visible, and I found this very simple technique sufficiently accurate to give constant results.

Fig. 12 is a curve obtained from fluid which was examined both before and after dialysis. The black (righthand) line is the absorption curve before dialysis, while the broken line (the lefthand curve) is that obtained after separation of the electrolytes. The dotted line is the normal curve of absorption.

After removal of the contained salts, by dialysis, the absorption is very much diminished, and, as will be seen from the graph, the hump has gone completely.

From my observations, it appeared that the typical humped curve of normal cerebrospinal fluid was due to the presence of the electrolytes in the

fluid, and that the removal of these tended to cause a disappearance of this hump—a flattening of the curve towards the short waves. In other words, the selective absorption gives place to a general absorption beginning somewhere about λ2350, but I have been unable to measure it accurately as it is just about the lower limit of the apparatus I was using. This result was surprising and quite different from what I had expected. The most striking changes in the absorption curve I had found had been in tuberculous meningitis, as mentioned above, where the curve is moved towards the long wave end of the spectrum, and it is in these fluids that there is a definite and well-recognized

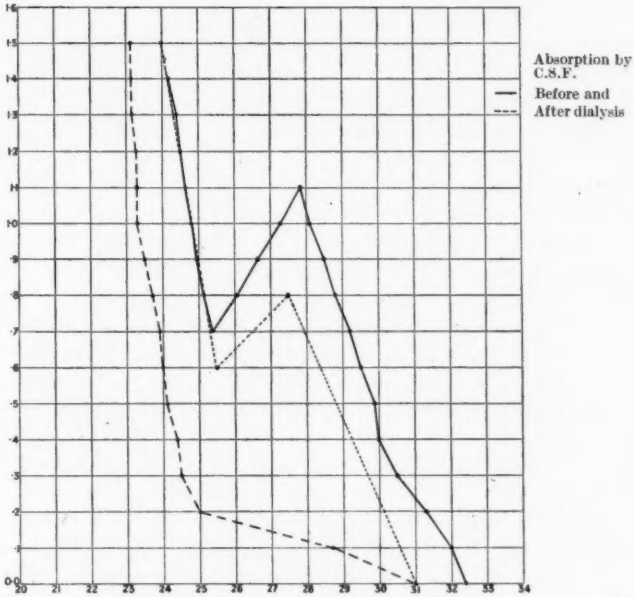

FIG. 12.—Dialysis experiment.

diminution in the chloride content; hence, if my observations were correct, and I had been at some pains to make them as reliable as possible, this fluid would be expected to produce a curve similar to that in dialysed cerebro-spinal fluid, which was obviously not the case. An explanation of this contradictory result might be found in a suggestion that there is some interaction between some of the electrolytes and other constituents of the fluid which may be responsible for the right-ward (long wave) shift in tuberculous cases, or that the influence of some such normal interaction which keeps the absorption curve towards the short wave end of the spectrum is removed and the remaining constituents are able, in the absence of electrolytes, to absorb more of the ultraviolet waves.

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FILTRATION OF CEREBROSPINAL FLUID

Another series of observations was carried out in an attempt to ascertain the type of curve obtained after the proteins had been removed by precipitation and subsequent filtration.

Here, again, the difficulty of dealing with small quantities of fluid and the necessity for keeping everything sterile became of still greater importance than in dialysis, since the manipulations were more frequent.

I used a small Chamberland filter candle about the diameter of a lead-pencil, and enlarged the bore at the open end, into which I placed the tapered end of a small 'thistle' funnel, connected to the candle with a short piece of rubber tube—merely to hold the two together. The candle was passed through a rubber bung which fitted tightly into a filter-flask with a side tube connected to the usual exhaust water-pump. The candle was then dipped into a small wide receiving tube placed inside the flask.

Before use, all this apparatus was sterilized and the small receiving tube, candle, and glass funnel were boiled in distilled water to ensure the absence of any added electrolytes, and distilled water was drawn through the filter for an hour to clear the candle of any salts, as far as possible.

The cerebrospinal fluid was boiled to precipitate the proteins (thus avoiding the addition of other electrolytes in the 'salting out' method). With a long sterile Wright's pipette, cerebrospinal fluid was passed down the bore of the candle (to displace air) and then about 3 c.cm. put into the funnel. (At least 3 c.cm. are essential, since some is lost in the filter, and one requires 1·5 c.cm. to ensure comfortable filling of the cells before spectroscopy.) Since another 1·5–2 c.cm. are required for the control spectroscopic examination and at least 5 c.cm. for the other routine tests, cell count, etc., the use of these very small filter candles is essential, as one cannot safely remove more than 8–10 c.cm. of cerebrospinal fluid as a routine measure.

Fig. 13 shows the type of curve resulting from spectroscopy in such an observation (*a*) before and (*b*) after filtration.

A number of such observations was made, and, as will be seen, the general appearance of these graphs (as exemplified in the one above) bears a close resemblance to the curves of meningitic fluids. In a case of meningitis following infection through a fractured base of the skull the curves obtained before and after filtration were so similar that removal of the protein appeared to have had very little if any effect.

The above observations seemed to point to the following conclusions.

1. Normal fluid absorbs the ultraviolet waves in a region between $\lambda 2600$ and $\lambda 3150$, giving the graphed curve a hump in this region.

2. Removal of electrolytes by dialysis prevents this absorption, as shown by the obliteration of the hump, the whole curve becoming horizontal and moved towards the left.

3. Removal of proteins has the opposite effect. It obliterates the hump by increasing the absorption and moves the curve to the right.

It will be noted that these conclusions are not what would have been expected from the observations obtained in various disease conditions noted previously. For example, in cases of tuberculous meningitis and general paralysis where the fluids have been more highly albuminous than normal, the curve of absorption shifts to the right and the hump is raised until the curve is practically vertical—in other words, a very similar type of curve to that obtained after removal of the proteins. It would appear then that highly albuminous fluids produce absorption of the same type as do fluids experimentally lacking in protein.

This discrepancy is very real and is difficult to explain, assuming that

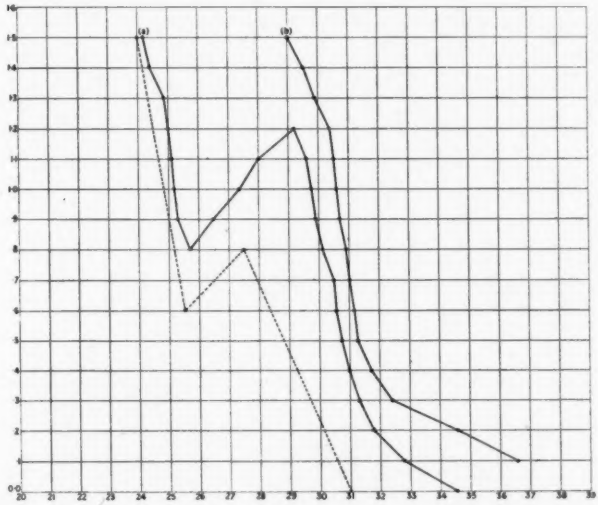

FIG. 13.—Filtration experiment. Absorption of ultraviolet waves (*a*) before filtration, (*b*) after filtration.

the technique of filtration is dependable. It may be that the presence of protein molecules holds electrolytes in such a way as to allow of a maximum absorption and that upset in this combination results in alteration in absorptive powers. Even this hypothesis is not completely satisfactory. Since from observations it follows that removal of protein produces a steeper curve, i.e. more complete absorption, it would seem that this must be due to the influence of the remaining electrolytes. Yet in tuberculous meningitis, where this extreme type of curve is found, the reduction of electrolytes is a definite factor, as shown by the diminished amount of chlorides present at any rate in the later stages.

The technique is admittedly open to criticism, and each observation must be made with a freshly cleaned filter, otherwise the most extraordinary results are obtained. The pores of the filter candle become choked with

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albuminous material and may actually add matter to the fluid instead of removing it.

Allowing for this difficulty, however, there remains sufficient concordance to suggest that there is some tendency to obliterate the absorption hump and shift the curve towards the long wave end of the spectrum.

ANALYSIS OF NORMAL CEREBROSPINAL FLUID ABSORPTION CURVE

The most outstanding feature of normal fluid is the presence of the band of absorption between λ2600 and λ3150, giving rise to the hump in the curve.

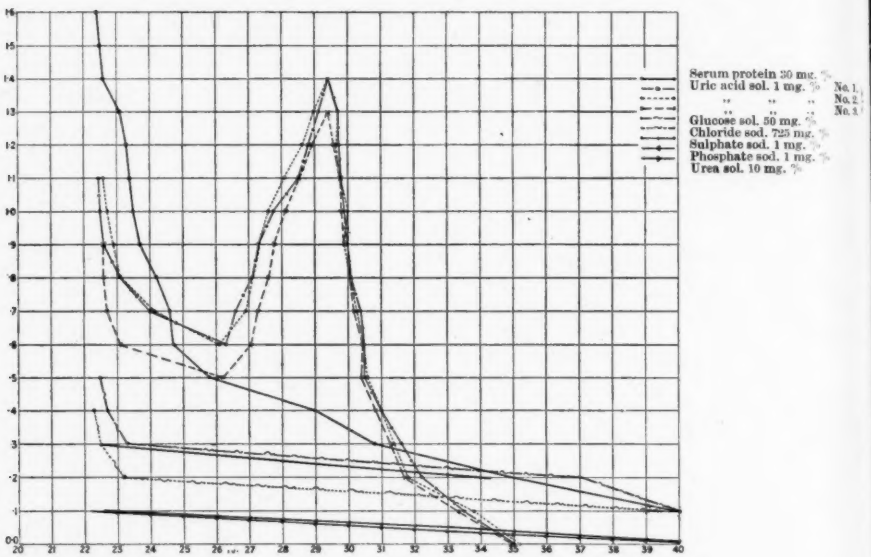
Serum protein 30 mg. %
Uric acid sol. 1 mg. %
No. 1.
" " " No. 2.
" " " No. 3.
Glucose sol. 50 mg. %
Chloride sod. 725 mg. %
Sulphate sod. 1 mg. %
Phosphate sod. 1 mg. %
Urea sol. 10 mg. %

FIG. 14.—Absorption of ultraviolet rays by the various constituents of C.S.F. dissolved in distilled water in the concentration found in normal cerebrospinal fluid.

When these experiments were first planned I thought that any alteration in the fluid would almost certainly be due to increase in the protein content and that the proteins would be likely to impart any characteristic feature of absorption. After working for some time, however, it became clear that such a priori views were wrong and an attempt was made to try and ascertain to what the hump was due.

After reviewing various statements about the chemical constitution of cerebrospinal fluid I selected the composition as given by Greenfield and Carmichael [7] as probably the most recent.

I proceeded to examine the spectrogram of each of the constituents, and fig. 14 is a composite graph of these absorption spectra.

It will be noted that with one exception all the electrolytes give a very similar absorption, which is almost nil, the curve being practically a horizontal line. The proteins again begin to show absorption only in the short wave-length region, similar to the electrolytes just mentioned, but there is a striking absorption between λ2600 and λ3200.

This was given by the last solution submitted to the test, namely, uric acid, a constituent which in some analyses is not even mentioned, and in those analyses which do mention it it is stated to be present in such small amounts as to be negligible. The spectrogram that I obtained was so different

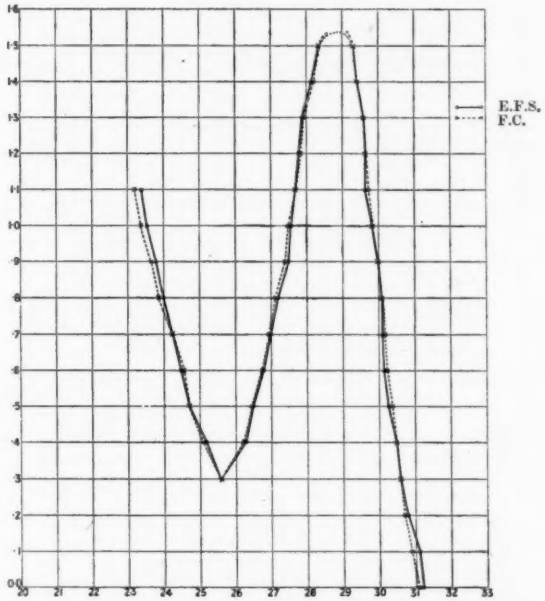

FIG. 15.—Absorption of ultraviolet waves by solution of uric acid (0·01 per cent.). Two observations on same sample of fluid by independent observers.

from what I had expected that I made repeated observations, but always with the same result. Three such observations are recorded on the graph in fig. 14.

The spectrophotometric analysis of solutions is not a particularly easy technique, and, as will be gathered from the description of the 'spotting' of negatives in the introduction, it depends on careful visual comparison of two slightly dissimilar degrees of photographic blackness. I realized the possibility of personal error in such examination, and in order to test what such error might be, I 'spotted' a spectrogram of a solution of uric acid 0·01 per cent. on the back of the negative, recorded this 'spotting,' and

rubbed off the spots. I then sent the negative to Dr. Simeon, one of the senior physicists at Messrs. Adam Hilger's, and he kindly allowed one of his trained staff to 'spot' the negative again. The negative was unmarked in any way. Fig. 15 represents the graph constructed from the two independent examinations of this negative.

It appears clear from this that the difference in personal variation of two individuals 'spotting' the same negative is very slight. I think therefore one can claim that this technique, once acquired, is probably less liable to

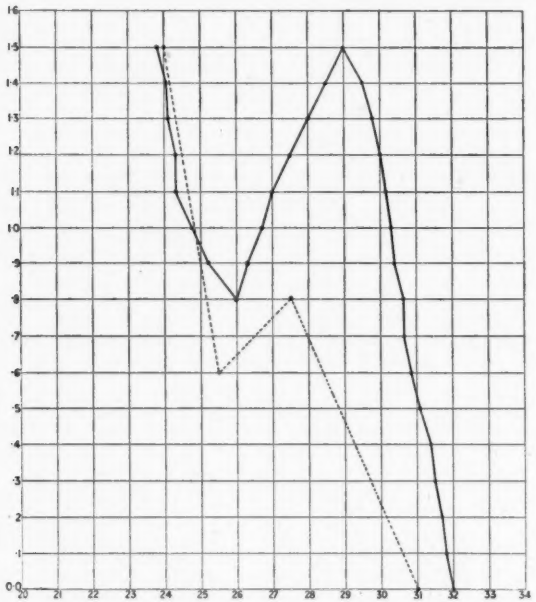

FIG. 16.—Absorption of ultraviolet waves by serum of normal blood. Absorption due to uric acid (after Campbell Smith). Similarity of absorption by C.S.F. suggests the same cause.

personal error than the estimation of, say, hæmoglobin in a routine blood count.

After a number of observations had been made from both normal and pathological fluids, it appeared justifiable to assume that the absorption of ultraviolet waves by cerebrospinal fluid in the region of wavelengths between $\lambda 2600$ and $\lambda 3200$ might be directly attributable to the minute traces of uric acid occurring in the fluid. If this absorption band, so noticeable in normal fluid, is due to uric acid (as seems possible), an increase in the amount present would be likely to increase the absorptive power of the fluid. Such an increase would tend to obliterate the hump in the curve and render it steeper by

shifting the curve towards the right end of the spectrum. In other words, there would be a tendency for an increased amount of uric acid to give rise to the meningitic type of curve.

In this connexion it is of interest to note Bernhard's[8] findings. In a series of 51 cases he has found that ' The average uric acid content, excluding cases of meningitis, is rather higher in children than in adults. In polioencephalitis and encephalitis lethargica rather high normal figures were found, e.g. 0·8, 0·88, 1·2 and 2 mgm., while in meningitis the readings were occasionally much higher still, up to 3·5 and 4·8 mgm.'

If one can accept the uric acid content as the cause of the shifting of the curve to the right, then the discrepancy between the observations of dialysis and filtration, noted previously, is largely explicable. Dialysis removes the salts, including uric acid, and a more or less horizontal curve is obtained (fig. 14) with a shift to the left, any remaining absorption being due to the protein. Filtration, on the other hand, removes the protein, leaving the salts, and the uric acid may now be able to exert more influence than when it is present in conjunction with protein in normal amount. In meningitis the absorptive effect of uric acid appears to outweigh that of the protein, although both constituents may be increased.

This type of curve, which on the evidence above might be assumed to be due to increased uric acid in the cerebrospinal fluid, is always associated clinically with coma, and it may be that the coma is a direct toxic action on the neurons of this high concentration of uric acid. It is of interest to note that a similar type of curve is found in cases of uræmia. Examination of a number of fluids from fatal cases of coma of various types—uræmia, cerebral hæmorrhage, lateral sinus thrombosis, etc.—gave absorption curves so similar to the meningitic curve that there arises the possibility that they may be all due to one factor and that uric acid may be the factor involved.

Campbell Smith,[9] working with blood serum, in 1928 found a curve of absorption for uric acid practically identical with the ones I have depicted above. In his work he filtered serum through a special membrane by a process of rapid dialysis,[10] and the resulting filtrate gave the absorption curve shown in fig. 16. By such a rapid method it is likely that some of the smaller protein molecules may have got through, as well as all the electrolytes, so that he was really producing a fluid practically identical with cerebrospinal fluid, which is, after all, a filtrate of blood serum through a similar membrane.

MISCELLANEOUS CASES

In January, 1935, there was admitted to one of my wards a young woman of about 25 years of age, deeply comatose, and of whom little could be learned at the time. She had been found unconscious at her work.

A lumbar puncture was done at once, and on examining the fluid spectro-

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graphically I obtained a curve rather like the early meningitic or syphilitic curve, but in its position on the graph also resembling the ' coma ' type. I was at first convinced of the uræmic nature of the coma, but clinical observation did not bear this out, and as she began to recover after about two days the diagnosis was left open.

It was learned later that she had tried to procure abortion (she was about three months pregnant) by taking some ' stuff ' given to her by her partner. She had no knowledge of what this ' stuff ' was, nor could we get any evidence from her parents.

The similarity of her condition and that of patients recovering from the effects of nembutal anæsthesia suggested that she might have been given one of this group of drugs. Accordingly I tried to arrange with a colleague, who has a licence, to inject nembutal into a rabbit and then draw off the cerebrospinal fluid and allow me to examine it with the spectrograph. Owing, however, to technical difficulties the observation was abandoned and I had to content myself with a substitute for it. I obtained several samples of normal cerebrospinal fluid and added to them varying percentages of both veronal and nembutal and then examined the spectrogram of each solution. A composite graph of this observation gave curves almost identical with that obtained from the comatose girl. It seemed likely therefore that she had been poisoned by one of the barbituric group, and this was afterwards confirmed by my colleague Dr. Webster, Police Surgeon for the City of Sheffield, who from other evidence had obtained proof of barbituric acid poisoning.

This observation seemed interesting in suggesting that with adequate safeguards and an assured technique the method might have a medicolegal value in the identification of drugs excreted by body fluids.

In hydrocephalic cerebrospinal fluid, in which the constituents are present in more minute amounts than normal (the fluid consisting practically of water), the type of curve is interesting, being similar to that obtained in a normal fluid after dialysis when all the protein is removed. There must be a trace of protein in the hydrocephalic fluid since filtration after boiling does make a slight difference, and that in the usual shift of the curve to the right.

Although only three or four observations have been made on hydrocephalic fluids as opportunity has offered, this fluid is so different from normal cerebrospinal fluid that I have introduced the observation as it appears to me to support the experimental results in dialysis and filtration mentioned above.

Several examinations have been made of fluid from cases of schizophrenia, but I have as yet failed to notice any definite characteristic in these cases. This is more or less in conformity with the conclusions of Jacobi and Winkler.[5] Unfortunately these two observers produce curves which, as they themselves admit, cannot be compared with those of other workers,

since instead of using the extinction coefficient as ordinate they employ the logarithm of the varying thickness of the fluid through which the light is passed.

In a more recent paper they [11] express the opinion that in early cases of schizophrenia the absorptive power is not very different from that of normal people, as I have found in the few cases I have examined, but that later in the progress of such cases the fluid does show changes in the direction of marked absorption increase. They conclude their paper by stating: 'Although our findings are not sufficiently secure to be used as a method of differential diagnosis, nevertheless we think that they have a special interest in connexion with the view gradually gaining ground that the schizophrenic process is associated with definite somatic changes.'

CONCLUSIONS

From the observations made in these experiments it appears that certain conclusions can be drawn; and though with better apparatus some of the details would probably be varied, the general tendency will, I think, be found to hold.

1. Normal cerebrospinal fluid has a definite absorption spectrum with a band of absorption between $\lambda 2600$ and $\lambda 3200$, which gives a humped curve on a graph.

2. In cases of infection of the meninges, whether acute or chronic, the normal curve is shifted towards the long wave end of the spectrum.

3. There appear grounds for believing that the hump in the normal curve may be due to uric acid and that the shift to the right in inflammatory conditions is possibly due to an increase in this constituent.

4. Certain observations seem to suggest that in some cases coma may be due to the direct action of uric acid on neurons.

5. Removal of electrolytes diminishes absorption and shifts the curve to the left, giving a horizontal-seeking curve.

6. Removal of protein has the opposite effect, giving increased absorption and a shift of the curve to the right.

7. There is some slight evidence that the method of ultraviolet spectroscopy might be of use in identifying substances excreted in body fluids.

I would particularly like to record my thanks to Dr. Simeon of Messrs. Adam Hilger's for much kindly help in the early stages of my experiments.

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ASSOCIATED FACIAL, VOCAL AND RESPIRATORY COMPONENTS OF EMOTIONAL EXPRESSION: AN EXPERIMENTAL STUDY *

By

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Among the topics which Kinnier Wilson [1] has selected as representing some modern problems in neurology is that presented by the clinical picture of dissociation of the voluntary and emotional innervation of the facial muscles. It has long been known that patients suffering a paralysis of volitional movement of the facial musculature, as a result of supranuclear cortical or capsular lesions, may retain an activity of these muscles in the expression of emotion. Conversely, cases have been reported in which voluntary activation of the facial muscles has been unimpaired, while emotional excitement failed to produce the appropriate facial expression.

In his review of this subject, Kinnier Wilson [2] has suggested in explanation that the voluntary and emotional innervations of the facial nuclei are effected by different systems within the brain. Enlarging upon this suggestion, Wilson has postulated a brainstem mechanism which subserves the synkinesis of the facial, vocal and respiratory activity observed in emotional behaviour. Further elucidation has been provided by Bard [3] in a consideration of facial and vocal activity from the point of view of his [4, 5] recent studies of the brainstem mechanisms involved in the expression of emotion.

Our interest in this problem has developed from a series of investigations of these brainstem mechanisms (Ranson et al.[6–13]), in the course of which we have repeatedly observed coordinated facial and vocal responses obtained as specific reactions to stimulation of localized areas within the brainstem of experimental animals. It seemed desirable to make a special study of these effects, and we wish now to report the results of an investigation of such responses obtained from systematic electrical stimulation of the brainstem of the lightly anæsthetized cat and monkey and of the acutely decerebrate cat.

METHODS

Data were obtained from eight monkeys (Macaca mulatta), from 14 normal cats, and from six cats decerebrated through the caudal part of or

* From the Institute of Neurology, Northwestern University Medical School. Aided by a grant from the Rockefeller Foundation.

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just behind the diencephalon. Of the eight monkeys, one was a normal animal, while each of the others had been the object of a previous study on the effect of restricted lesions in the hypothalamus or thalamus. No significant variation could be detected in comparing the results from the operated monkeys with each other or with those from the normal monkey.

The monkeys and normal cats were given nembutal (16 to 20 mg. per kilo body weight, intravenously) to preserve a light anæsthesia, and under supplementary ether the skin was incised, the appropriate region of the calvarium was removed, the dura reflected, and the Horsley-Clarke instrument adjusted to the animal's head. The decerebrate cats were prepared by the transection method under ether which was discontinued after decerebration. All brain tissue ahead of the plane of transection was removed at operation in the decerebrate animals, the level of section was described and drawn at autopsy, and in two instances was determined by microscopical examination of serial sections of the intact end of the brainstem.

In one monkey kymographic records of the respiratory changes associated with the responses were made, and it may be emphasized that this was the only animal of the series in which a tracheal cannula was employed. Reactions from this animal were checked for vocal effects, however, by stimulation of each point concerned either before insertion of the tracheal cannula, or after its removal and closure of the trachea by inserting and tying in a short length of glass tube to divert the air once more through the larynx.

All stimulation of the brainstem was performed with the aid of the Horsley-Clarke instrument, the use of which has been described in detail by one of us.[14] The short distance, approximately 0·2 mm., between the electrodes used, together with the weak faradic current from one dry cell attached to a Harvard inductorium the secondary coil of which was set at 9 cm., permitted restriction of the stimulation to a localized area surrounding the tips of the electrodes.

The region explored extended in the monkey from the transition between thalamus and midbrain, through the midbrain, to the upper part of the medulla, and included the entire left half of the brainstem and the medial portion of the right side, all or a large part of this region being explored in each of the animals. In some, stimulation was begun rostrally and extended caudally; in others the reverse procedure was followed. Stimulation of the brain in the normal and decerebrate cats was in each case begun rostrally and extended caudally, exploration being made of the left side of the brain and the medial portion of the right side. In the normal cats the anterior part of the cerebral hemispheres and the diencephalon were explored in some animals and the diencephalon, midbrain and pons in others. In the decerebrate cats, exploration was necessarily confined to the midbrain, pons and upper part of the medulla.

Extensive written records of the responses were made throughout the course of each experiment, and the site of each focus of stimulation was

determined by subsequent microscopical examination of serial sections of the explored area of the brain prepared for histological study by the Weil method. This location of the reactive points was first determined for each animal on projection drawings of sections through the explored areas. Representative levels were then selected and the data from all of the animals explored in these planes were plotted upon them. Four such levels shown in figs. 2–5 illustrate the localization of reactions in the monkey, and those shown in figs. 6–14 the localization in the normal and decerebrate cats.

OBSERVATIONS

Description of responses from the monkey.—Vocalization in the monkey occurred rhythmically with each expiratory phase of a greatly accelerated respiration. It has most commonly been manifest as cries of a wide variety of intensity and pitch, ranging from soft and plaintive sounds, through moderately loud and high-pitched notes, to loud shrill shrieks or screeches. Another large number of responses may be described as barking of a chirruping or chattering nature. Occasionally cooing or whistling sounds have been encountered. With the exception of these rare cooing or whistling noises, the sounds as a whole have impressed us as resembling those which connote the expression of unpleasant affective states, and a large number of the responses have closely simulated examples of the rather extensive repertoire of vocal expressions exhibited by the normal monkey in the emotional behaviour of its daily life.

The play of the facial muscles, which was an accompanying feature of the majority of these vocal responses, also resembled closely that seen in the activity of the normal monkey, with the difference that it was usually present only on one-half of the face, that contralateral to the side of stimulation. Much less commonly bilateral or ipsilateral contractions of the muscles of expression were encountered. In addition to the accompanying opening of the mouth and dilatation of the nostrils, the responses of barking and crying were most commonly associated with a contraction of the facial muscles producing a retraction of the angle of the mouth, an elevation of the upper lip, and to some extent the side of the nose. As a result of these contractions the teeth were exposed and the face assumed a snarling expression. Less commonly the forehead was wrinkled, and the ears retracted and flattened against the side of the head. These facial contractions were not tonic ones but occurrred phasically and in definite patterns with each expiration and cry, being partially or completely relaxed during inspiration. The less frequent whistling sounds and some of the soft, chirruping barks were not accompanied by movements of this sort, but instead were associated with a contraction of the lips to produce a rounding of the mouth-opening, which appeared not so much a grimace as an aid to phonation.

Irrespective of the specific nature of the vocalization or facial expression

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two general types of responses have been obtained. In the first of these, the vocal effects did not occur at the onset of stimulation, but appeared only after the stimulus had been continued from one to several seconds, there often being an initial apnœa. Vocalization began with soft and low-pitched cries or barks, and the succeeding sounds, occurring with each expiration, became increasingly louder and higher pitched as excitation was continued. At the cessation of stimulus, there was usually one, but sometimes several cries or barks still louder and higher pitched than those elicited during stimulation.

A kymographic record of the respiratory changes associated with this type of response is shown in fig. 1A. Before stimulation in this record, the

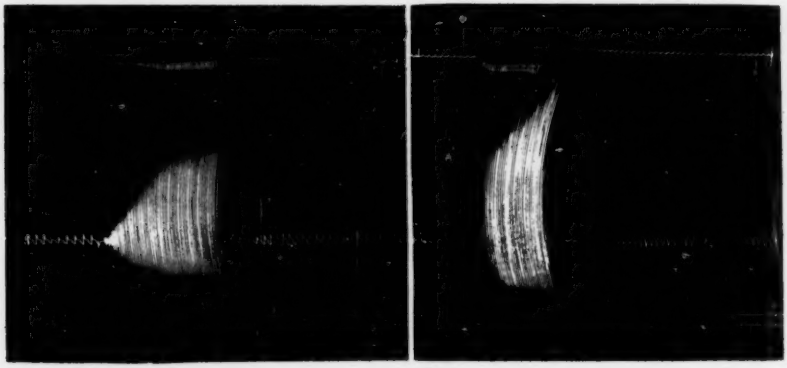

Fig. 1.—Kymographic records of respiratory changes associated with vocal responses from the monkey. The tracings from above downward represent : chest movements with expiration as a downstroke ; air exchange from tracheal cannula with expiration as an upstroke ; a signal-marker with the dip indicating the period of stimulation ; and the time in three-second intervals. Record A illustrates the response to stimulation of a point in the central grey matter of the aqueduct ; record B the response to stimulation of a point in the lateral part of the mesencephalic tegmentum.

respiratory rate was 48 per minute. Respiration was partly inhibited for the first second of stimulus, and then began and continued for the duration of stimulus at a rate of 224 per minute, gradually increasing in amplitude during the first half of the period of stimulation. After faradization was stopped there occurred one respiratory excursion comparable to those seen during stimulation. The vocal effects elicited from stimulation of this same point before insertion of the tracheal cannula appeared shortly after the beginning of stimulus, starting with low cries. The succeeding cries, occurring with each expiration, became increasingly louder and higher pitched as stimulation was continued, and at the cessation of stimulus there were one or sometimes two cries still louder and higher pitched than those obtained during faradization.

Reactions of this type are characterized in brief by an initial apnœa, a

gradual appearance of the excitatory effects and their increasing development with continued stimulation, together with a post-stimulatory component. It will be made clear below in the section on localization that these responses were obtained only from a part of the reactive area within the brainstem.

In the second general type of reaction, the vocal effects appeared with no appreciable latent period at the onset of stimulation, continued at the same intensity and pitch throughout stimulus, and ceased at its conclusion. A record of the respiratory changes associated with this type of reaction is shown in fig. 1B. In this record, the amplitude of respiratory excursion increased throughout the period of stimulation, but there is no evidence of the inhibitory influence which the first record may be interpreted as showing. Before stimulation in fig. 1B, the respiratory rate was 53 per minute, and during the 11 seconds of stimulation it was increased to a rate of 188 per minute. After cessation of the faradization there were no excursions comparable to those seen during stimulus. The vocal effects, elicited from this same point after removing the tracheal cannula and inserting and tying in a short length of glass tube to close the trachea, consisted of high pitched cries with each expiration. These began at the onset of stimulation and stopped at its conclusion, the successive cries remaining of the same intensity and pitch throughout.

Localization.—The location of the foci whose stimulation has produced the responses which have been described are shown in four levels through the brainstem of the monkey (figs. 2–5). Correlated facial and vocal reactions are indicated by solid black symbols, vocal effects alone by outline symbols. Soft cries are shown by circles, loud cries or screeches by squares, and barks by triangles. It can be seen that the reactions have been obtained from a large part of the rostrocaudal extent of the central grey matter of the aqueduct, from the dorsal part of the tegmentum of the midbrain, together with its lateral and ventral parts in the midbrain and pons, and further caudally and ventrally from the lateral part of the reticular formation of the upper medulla.

The different vocal expressions do not appear to have any specific localization within the reactive area in the central grey matter and mesencephalic tegmentum, but responses of the first type which may be interpreted as due to the stimulation of mixed excitatory and inhibitory elements (fig. 1A) have been obtained only from the central grey matter or the immediately adjacent dorsal portion of the mesencephalic tegmentum. The reactions from this region were not exclusively of this type, however, for responses of the second type (fig. 1B), which show only an excitatory effect, have been obtained in part from the central grey matter and the adjacent tegmentum. Reactions of this second type are the only ones obtained from the ventrolateral part of the tegmentum and its continuation in the reticular formation of the medulla.

Changes in facial expression are seen to have had a fairly regular distribu-

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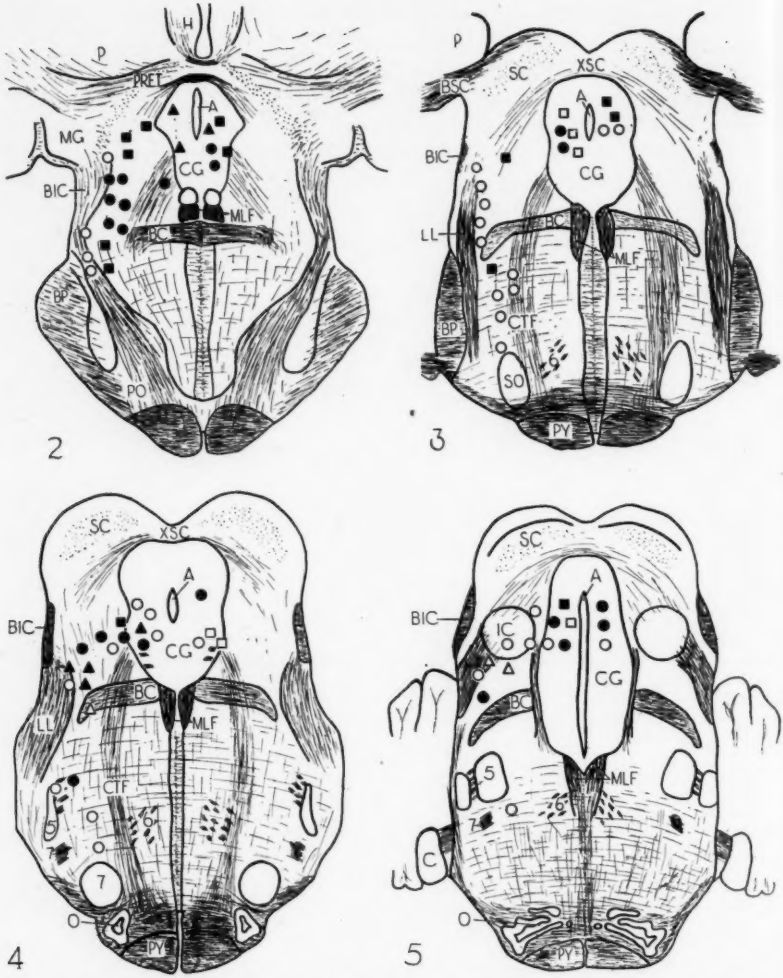

Figs. 2-5 illustrate the location of points whose stimulation produced faciovocal effects from the lightly anæsthetized monkeys. The four levels through the brainstem are in the vertical plane of the Horsley-Clarke coordinates and extend serially from the most rostral to the most caudal plane. These planes are oblique from the transverse because of the angle given to the caudal part of the brainstem by the cephalic flexure of the monkey brain. Each level shows the data from three animals. Correlated facial and vocal effects are indicated by solid black symbols, vocal effects alone by outline symbols. Soft cries are shown by circles, loud cries or screeches by squares, and barks by triangles. Abbreviations for figs. 2–13 are as follows :

A	**aqueduct**
BC	**brachium conjunctivum**
BIC	**brachium of inferior colliculus**

tion among the responses through the midbrain, but were not frequently elicited from the pons and never from the upper part of the medulla. It has already been noted that these changes were seen predominantly in the crossed side of the face. The data, however, do not furnish any information as to the site of the crossing. Direct stimulation of the facial nucleus or the facial nerve, anywhere along its devious course through the brainstem, yields only a coarse clonus or subtetanus of all or several of the ipsilateral facial muscles, the rate of contractions apparently being related to the frequency of induction shocks. Such responses may be readily distinguished from changes of expression, the latter being predominantly or entirely of the crossed side of the face, of a rate synchronous with respiration, and selectively involving definite groups of facial muscles to produce characteristic grimaces.

Systematic stimulation of the transition area from thalamus to midbrain in the monkey, rostral to the level shown in fig. 2, has not yielded any faciovocal effects. Exploration of the thalamus or hypothalamus has not been attempted in these experiments. There appeared to be a definite dropping out of the responses as the upper part of the medulla was reached, though no comprehensive exploration of the remainder of the medulla was attempted in these animals. In considering the significance of such negative data, the possibility should be kept in mind that areas which are non-reactive may contain functionally important cells or fibres which are too scattered to be effectively activated by the localized stimulus employed.

These faciovocal responses obtained from the monkey cannot be considered as isolated phenomena peculiar to this animal alone, for comparable

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BP	brachium pontis
BSC	brachium of superior colliculus
C	cochlear nucleus
CG	central grey matter
CTF	central tegmental fasciculus
H	habenula
IC	inferior colliculus
IV VEN	fourth ventricle
LL	lateral lemniscus
LM	medial lemniscus
MG	medial geniculate body
MLF	medial longitudinal fasciculus
O	inferior olive
P	pulvinar
PE	basis pedunculi
PO	pons
PRET	pretectal region
PY	pyramidal tract
RN	red nucleus
SC	superior colliculus
SN	substantia nigra
SO	superior olive
XIC	commissure of inferior colliculus
XSC	commissure of superior colliculus
5	fifth nucleus or nerve
6	sixth nerve
7	seventh nucleus or nerve

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effects have been elicited from stimulation of a similar region of the brainstem of the cat.

Description of reactions from the cat.—Two general groups of responses were obtained from the cat, the first being made up of cries and the second consisting of spitting reactions. The cries obtained varied widely in pitch, and ranged in intensity from soft and almost sighing effects to loud wails and howls, or intense screams. The prolonged duration of each cry was a characteristic feature. These cries were successively repeated during the period of stimulation, sometimes regularly with each expiration, but usually with from one to three silent respiratory excursions, or a period of respiratory inhibition between cries. Commonly also, they occurred alternating with from one to four spitting responses. While these effects sometimes appeared only after latent periods which could be estimated in periods of seconds, they have usually been manifest with no appreciable latency at the onset of stimulation. Only rarely has an increase in intensity or pitch of the cries during the period of stimulation been observed.

Even the most vigorous of the cries from the cat have characteristically been obtained with a minimum of noticeable alteration in the musculature of the face and mouth. With rare exceptions, they definitely were not accompanied by any emotional play of the face. Usually the mouth was opened slightly, and sometimes the tip of the tongue was retracted with each expiration and cry. Rarely a slight tensing or tremor of the lips was observed.

The spitting reactions from the cat exhibited, on the other hand, a minimum of vocalization associated with vigorous contractions of the muscles of the face, jaw and tongue. In these spitting reactions the mouth was opened widely, the back of the tongue was elevated, and its sides were tipped upward to form an elongate trough of the anterior portion. The angles of the mouth were retracted and the upper lips elevated, exposing the formidable canine teeth. The muscles on the side of the nose were contracted to pull the tip of the nose upward and the skin of the forehead downward. Occasionally the ears were retracted and flattened against the head. All of these contractions were performed phasically and in a coordinated manner with each expiration, which was audible as a short and often explosive hiss. They were partially or completely relaxed during inspiration. The facial contractions were sometimes bilateral and equal, but were often more marked on the half of the face opposite the side of stimulation, and were sometimes exclusively contralateral. The respiratory rate was usually accelerated.

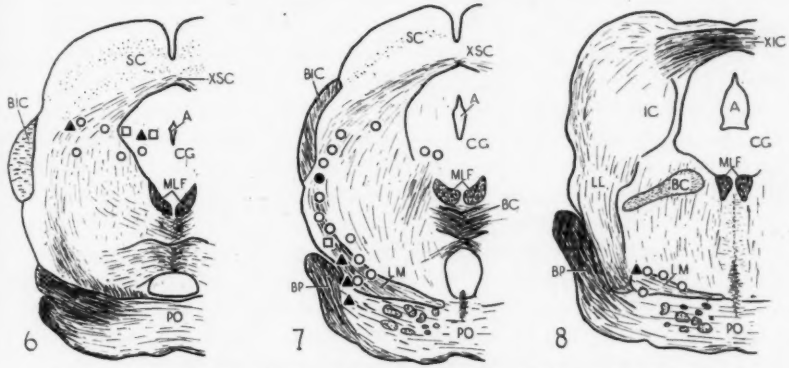
The contrast in the emotional play of the face during the crying and the spitting reactions was strikingly illustrated when the two occurred on alternating expirations during stimulus. With the cries the face remained still and expressionless, while with the spitting it exhibited the activity just described.

The responses from the cat, like those from the monkey, have impressed

us as resembling those which connote the expression of unpleasant emotions. Also, as in the case of the monkey, a large number of reactions from the cat have so closely resembled the facial and vocal activity of the normal animal during emotional behaviour in its daily life as to appear identical with it.

Localization.—The location of the points whose stimulation has produced the responses from the normal cats is shown in three levels through the brainstem of that animal (figs. 6–8). Correlated facial and vocal effects are indicated by solid black symbols, vocal effects alone by outline symbols. Weak cries are shown by circles, loud cries or screams by squares, and spitting by triangles.

The responses have been obtained from the rostral portion of the central



Figs. 6–8 illustrate the location of points whose stimulation produced faciovocal reactions from the lightly anæsthetized cats with intact brain. The three levels through the brainstem are in the vertical plane of the Horsley-Clarke coordinates, 6 being the most rostral level and 8 the most caudal. Figs. 6 and 7 each show the data from three animals, level 8 that from two animals. Correlated facial and vocal effects are indicated by solid black symbols, vocal effects alone by outline symbols. Weak cries are shown by circles, loud cries or screams by squares, and spitting responses by triangles.

grey matter surrounding the aqueduct, and the reactive area extends from this region through the dorsal portion of the mesencephalic tegmentum to its lateral part (fig. 6). At a more caudal level (fig. 7), reactions have been obtained from the areas just described and in addition from the extent of the lateral and ventrolateral boundaries of the mesencephalic tegmentum. Still further caudally (fig. 8), responses were elicited only from the region of the fibre-bundles forming the ventral boundary of the tegmentum.

The different vocal expressions do not appear to have any specific localization within the reactive area, but responses in which there was a period of respiratory inhibition between cries were obtained only from the lateral edge of the central grey matter and the adjacent dorsal portion of the mesencephalic tegmentum.

Mention has been made in the introduction that responses comparable

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to those just described have often been encountered before in investigations in this laboratory ; but in many of these investigations, particularly in those on the forebrain, use of a tracheal cannula has precluded any possibility of studying vocal activity. In the present experiments without a tracheal cannula the opportunity was taken, therefore, of reexploring the more rostrally situated parts of the brain for associated facial and vocal reactions. Stimulation of a large number of points in the anterior part of the cerebral hemisphere, including the anterior limb of the internal capsule, the septal region and a large part of the corpus striatum, did not yield any such responses.

A reactive region was encountered, however, in the anterior part of the hypothalamus from about the level of the supraoptic commissures to that of the ventromedial hypothalamic nucleus, and included the region of the lateral hypothalamic area, the subfornical component of the medial forebrain bundle, and the nuclei supraopticus diffusus, perifornicalis and hypothalamicus dorsomedialis.

From this region spitting responses were elicited which were identical with those obtained from the midbrain. Stimulation within this area also produced a variety of cries entirely comparable to but generally of less intensity than those obtained from the midbrain. In one animal, stimulation within this portion of the hypothalamus produced purring, a response we have never encountered from the midbrain. There has been no specific localization of the different reactions within the responsive area, and the situation from which the variety of responses has been obtained in these experiments is identical with that found to yield spitting reactions in earlier investigations (Ranson and Magoun,[8] Kabat [13]). This location has been well illustrated in fig. 9 of the paper by Kabat,[13] to which reference is directed. Aschner [15] and Karplus [16] have previously induced crying by stimulation of the hypothalamus, and Gibbs and Gibbs [17] have elicited purring from electrical stimulation of the infundibular region. The vocalization reported by Bechterew [18, 19] from thalamic stimulation in the guinea-pig, rabbit, cat and dog has little localizing value, since the entire diencephalon was often enclosed between the electrodes.

Stimulation of the caudal portion of the hypothalamus in the present series of experiments yielded no facial or vocal reactions and no connected chain of responses could be traced from the hypothalamus into the reactive area in the midbrain. Here, again, the possibility should be kept in mind that negative results may be due to such factors as scattered pathways or the effects of anæsthesia.

The responses to electrical stimulation within such a complex part of the nervous system as the brainstem cannot be distinguished a priori as being due to the activation of afferent or efferent pathways or systems. Reference to neuroanatomical information concerning the reactive structures is often of help in deciding this, but when applied to the site from which

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faciovocal reactions have been obtained from the midbrain and pons of the cat and monkey in these experiments it is of little aid, for the reactive area as a whole does not correspond to the distribution of any well-defined anatomical pathway or system familiar to us. The relation of some of the responses on the ventral and ventrolateral aspects of the tegmentum (figs. 7, 8) to the medial lemniscus, in association with which the spinothalamic fibres ascend, suggests the possibility that the responses were produced by stimulating afferent fibres coursing through this region to the thalamus. In an effort to explore this possibility, the midbrain and pons were stimulated in six cats in which the attempt was made to eliminate any participation of such afferent fibres by transecting the brainstem just behind the diencephalon. This procedure also eliminated afferent arcs relayed to the cerebral cortex.

Reactions from the decerebrate cat.—In only one of these cats could the diencephalon be considered entirely eliminated, its caudal and ventral parts remaining intact in the other five. We observed the occurrence of typical faciovocal responses to stimulation of the midbrain and pons in all of the decerebrate animals. The reactions consisted of cries and spitting reactions so identical in every respect with those elicited from the lightly anæsthetized cats with intact brains, as described above, that a second description would be superfluous. A slightly larger number of the more intense responses, as the screaming cries, were obtained from the decerebrate cats, but this difference was not marked and might be explained by the absence of anæsthesia in the decerebrate animals.

Localization.—The foci whose stimulation yielded the responses from the series of decerebrate animals are shown in six levels through the brainstem of the cat (figs. 9–14). The symbols have the same significance as in the case of the normal cat, and the identical distribution of the reactive areas in the normal and decerebrate animals is apparent (compare figs. 6–8 with 9–14).

As in the lightly anæsthetized cat with intact brain, responses of the decerebrate animals have been obtained (figs. 9–14) from the central grey matter of the aqueduct in the rostral portion of the midbrain, and extend from this region through the dorsal portion of the mesencephalic tegmentum to its lateral part. A number of responses are situated along the lateral boundary of the tegmentum, and at more caudal levels this reactive area becomes situated more ventrally and medially, so that in a plane through the inferior colliculus and rostral portion of the medulla it has assumed a position in the fibre-bundles on the ventral border of the transition from the tegmental region to reticular formation.

Responses from the lateral and ventral portion of the mesencephalic tegmentum whose possible relationship to spinothalamic fibres has been referred to above, have been obtained from all six of the animals of the decerebrate series, including one in which all diencephalic tissue was lacking, and a second in which the section passed from just behind the habenulæ to just in front of the mammillary bodies, and in which, therefore, only

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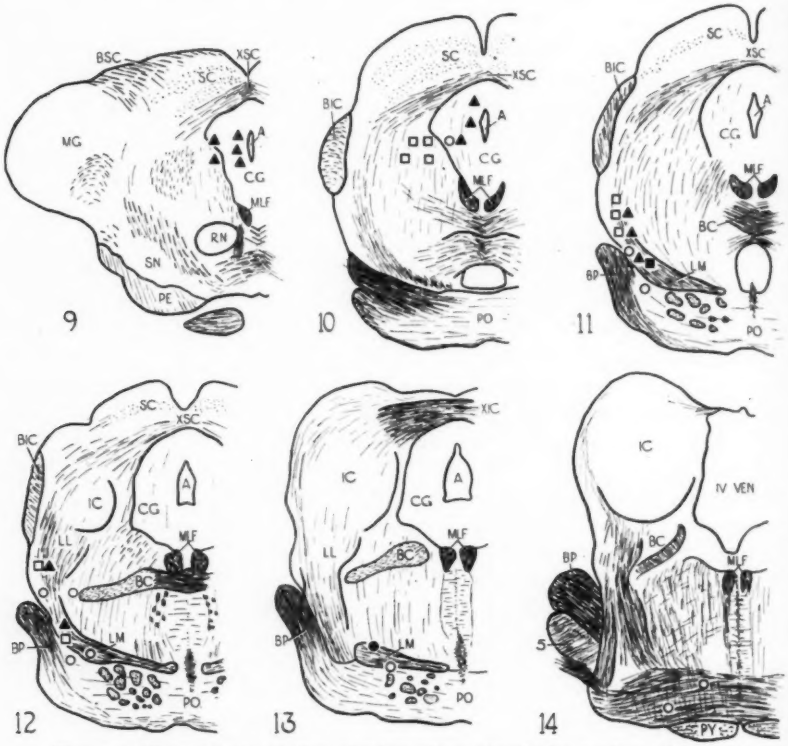
the most caudal portion of the diencephalon remained attached to the midbrain.

Reactions from the central grey matter of the aqueduct and the dorsal portion of the mesencephalic tegmentum were not obtained from the two animals just described, nor from one animal decerebrated through the



Figs. 9–14 illustrate the location of points whose stimulation produced faciovocal responses from the decerebrate cats. The six levels are in the vertical plane of the Horsley-Clarke coordinates and extend serially and caudally from the most rostral level, 9, to the most caudal, 14. Figs. 9 and 10 each show the data from two animals ; levels 11 and 12 each show the data from three animals ; levels 13 and 14 each show the data from one animal. The symbols represent the same responses as in figs. 6–8.

habenulæ dorsally and the infundibulum ventrally. They were elicited in abundance, however, from another animal transected through the habenulæ and infundibulum, and from a second animal in which the transection was adjacent to but slightly more anterior to this plane. They were also obtained from the central grey matter and dorsal tegmentum on both sides of the midbrain of a third animal in which the section had passed from just in

front of the superior colliculus on one side and a little farther forward through the caudal part of the thalamus on the other, downward and forward to just behind the optic chiasma ventrally.

Responses have been obtained from the central grey matter and dorsal tegmentum, therefore, in animals in which varying portions of the caudal part of one or both sides of the thalamus and hypothalamus have been present, but they have not been obtained from other animals in which the caudal part of the diencephalon has remained intact or in which the transection has passed just behind the diencephalon. These variable negative data should not be overlooked, but it may be questioned whether they are significant beyond indicating that the extent to which nervous tissue adjacent to a transection recovers its excitability may vary in different animals.

DISCUSSION

In considering the reactions obtained during these experiments, it should be pointed out that while cries have been obtained from both monkey and cat, these cries have not been identical in inflection and tone in the two animals. Each animal has, furthermore, yielded vocal responses specifically characteristic of its group alone, for barking has been elicited only from the monkey, and spitting only from the cat. Such differences are not, however, greater than might be expected of reactions from two widely separated species of animals, each of which has certain characteristic modes of emotional expression. In our opinion both the vocal and the facial reactions from the two animals represent components of a fundamentally similar response. A comparison of the regions of the brainstem from which the reactions have been obtained in the two animals permits one to go further and ascribe them to the stimulation of an essentially similar collection of neurons or their processes.

The fact that Graham Brown [20] obtained an apparently related type of reaction from stimulation of the cut surface of the central grey matter surrounding the transition from third ventricle to cerebral aqueduct in the decerebrate chimpanzee, in which all but the most dorsal and caudal part of the diencephalon had been removed, suggests that a similar mechanism for faciovocal responses may exist in higher primates.

There is little information concerning the nature of the reactive area. The fact that responses have still been obtained after elimination of the diencephalon by transection demonstrates that afferent connexions to the thalamus or higher centres are not essential. Such results from decerebrate animals do not exclude the dependence of these reactions on possible ascending pathways completing their afferent arcs at a mesencephalic level, and other investigators have reported reflex vocalization, in some instances with associated facial changes, occurring in acute and chronic midbrain preparations (Woodworth and Sherrington,[21] Bazett and Penfield,[22] and Keller [23]).

Such observations, however, attest the presence of an efferent mechanism of this type in the brainstem below the diencephalon, and it seems clear that within the reactive area delimited in these experiments there is contained an efferent pathway or system capable of producing facial and vocal responses during emotional excitement.

While the faciovocal reactions obtained from the midbrain and pons during these experiments have often been accompanied by such manifestations of general emotional excitement as pupillodilatation, pilomotor activity, urination, struggling, and, when it has been recorded, by rises in blood pressure, they have often occurred without any noticeable associated effects, or in association with responses whose emotional connotation is remote, such as the tegmental response of the limbs and trunk. It seems probable that a correlation of the faciovocal component with other features of emotional expression in the behaviour of the normal animal involves the activity of the more rostrally situated diencephalon or cerebral cortex.

SUMMARY

Coordinated facial and vocal activity, on the whole closely resembling that seen and heard during the expression of unpleasant emotion by the respective normal animal, has been obtained in response to electrical stimulation of a localized area in the midbrain and pons of the lightly anæsthetized monkey and cat, and of the acutely decerebrate cat. The anterior portion of the hypothalamus has also been found to be reactive in the lightly anæsthetized cat.

In both the cat and the monkey the reactive area in the midbrain includes the central grey matter of the aqueduct and a bridge of tissue extending from this region through the dorsal part and into the lateral and ventral portions of the tegmental area.

Responses from the decerebrate cat demonstrate that the effects are, in part at least, independent of afferent projections to the thalamus or cerebral cortex, and the conclusion seems justified that within the reactive area is contained an efferent pathway or system for eliciting coordinated facial, vocal and respiratory activity during the expression of emotion.

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PAROXYSMAL TRIGEMINAL PAIN WITH TUMOURS OF THE NERVUS ACUSTICUS *

By

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In 1910 Weisenburg [1] published a communication under the title 'Cerebellopontine tumour diagnosed for six years as tic douloureux.' This was the first recorded case of a particular type of pain associated with acoustic neurofibroma. The next important phase in the study of this particular tumour was Cushing's [2] book *Tumours of the Nervus Acusticus* in 1917. In the series Cushing reported including 30 cases of the disease there were only four cases where there was any complaint of pain at all. In none of them was pain conspicuous, persistent, or in any way like that associated with tic douloureux. In 1928 I [3] made a study of 53 cases of tumours of the acoustic nerve. Only those cases were taken in which the diagnosis had been established by microscopic study of tumour tissue obtained either at operation or at necropsy. In each case there had been a neurological examination and a careful study to determine the degree of involvement of the fifth nerve. In only four cases in the entire series was there any disturbance of sensation which could be described as pain. In only one of these four was the pain a dominant and persistent symptom and one which played the major part in the patient's complaint of symptoms. In the remaining three pain was only transitory and not conspicuous during the course of illness.

In the case of the one patient who had persistent pain the interesting feature was that the type of pain corresponded exactly to the syndrome known as tic douloureux. The earlier signs of deafness and nystagmus were inconspicuous, and of more interest still was the fact that the pain became relieved by the usual treatment for tic douloureux, namely, injection of the nerve with alcohol. It was only later with the advent of vomiting, ataxia and vertigo, that the true nature of the patient's condition was appreciated. To this experience, two more examples may be added.

A man, age 46, was seen by me in April, 1936, because of pain in the left upper and lower jaws. He stated that the previous seven years he had had recurrent attacks of fainting and vomiting. On one occasion he had been unconscious for from one to two hours, but there were no convulsive movements during the unconscious period. Three years before he had noticed a ringing and buzzing sound in the left ear associated with a progres ive deafness. A few months later he complained of

* Read before the Association of British Neurologists, June 12–13, 1936.

darting and stabbing pains in the canine tooth of the left upper jaw. Removal of the tooth produced no relief, and touching the lip or gum in the same region would initiate a paroxysm of pain. More teeth were removed without apparent benefit. He had remissions and exacerbations of this difficulty up to the time of his examination, and on one occasion was free from pain for at least eight months. A year before examination the pain spread from the upper jaw into the lower, and talking, eating, shaving, or washing his face when the pain was present would initiate a paroxysm. The paroxysms never lasted longer than 60 seconds, and pressure on the lower jaw seemed to produce relief.

During the six months previous to his examination many other symptoms appeared. He had attacks of vertigo, paroxysmal in character, and during at least a few of these attacks he fell to the ground. During the attacks of vertigo he had double vision, but a few weeks prior to his examination his vision had become generally poor, and he could not recognize people across the street. His gait was becoming progressively unsteady so that he walked as if he was drunk, and headaches appeared chiefly in the occipital region. With all these complaints his chief concern was the pain in his upper and lower jaws.

He was a well-built, burly, florid-complexioned man who presented himself with a reeling, staggering gait. There was complete deafness in the left ear and the corneal reflex was absent on the left side. There was nystagmus on lateral gaze more marked to the left than to the right, and both optic nerve heads were swollen—about one and one-half diopters on the right side and one diopter on the left. There was a slight hypæsthesia on the left side in the second and third divisions of the left nerve. The finger-nose test showed incoordination of both upper extremities, more marked on the left side. The same was true of both lower extremities, and his gait was ataxic with a certain degree of tilting of his head to the left side. The plantar reflex on the left side was extensor in character.

The diagnosis was made of left acoustic neurofibroma, and operation was advised. The patient did not consent to this treatment and left for home.

Pain in the area supplied by the fifth nerve was the dominant complaint of this patient. Similar to the previous case described by me, other complaints of vertigo, ataxia, deafness, and tinnitus seemed of less importance. Generally speaking, the case was otherwise a typical one of acoustic neurofibroma. Alcohol injection was not advised, for it seemed more important to attack the primary difficulty.

A woman, age 52, was examined in March, 1936. Her chief difficulty was attacks of pain in the right side of her face. As a secondary complaint, she had marked difficulty in walking, due to ataxia. It was difficult to obtain a coherent history because of repeated attacks of severe pain, making talking laborious. About five years before she had noticed deafness in her left ear, and with this there were headaches and staggering. At the hospital where she was examined she was given a course of X-ray treatments to her head. This relieved the headaches, but she complained that her gait was becoming more and more unsteady, and this continued during the years that followed. Six months previously, however, the pain in her face began, and from then on this was her chief complaint. The pain was located just above and to the lateral side of the right angle of her mouth. From there it radiated upwards into the right eye and right temporal region. The pain was sudden, sharp, severe, and of a burning character. It was initiated by movement of any kind, and while the paroxysms of pain were short in duration, she dreaded their occurrence so much that she lay for days immobile in bed. She preferred to keep her eyes closed, for she

found that raising the upper lid started the paroxysms. She had occasional remissions of pain of no longer than a week in duration.

At the time of the examination she was confined to the bed, and she was having one paroxysm of pain after another. She seemed to think that opening her eyes increased the pain, but with a little patience there could be established a nystagmus in all directions. Corneal sensation could not be tested because of the blepharospasm and pain. She was completely deaf in the left ear, but there was no facial weakness. The right patellar reflex was greater than the left, but plantar responses were flexor in character. There was no anæsthesia of the face, and the fundi were normal. After some persuasion she consented to walk, and there was a marked ataxia with a tendency to hold the head tilted to the left. The finger-nose test showed incoordination in both hands, more marked on the left side. The same was true in similar tests applied to both lower extremities.

The diagnosis was difficult because of the poor cooperation of the patient. Disseminated sclerosis and acoustic neurofibroma were considered. In the hope of securing better cooperation, relief of pain was obtained by injecting the second and third divisions of the right fifth nerve with alcohol. This was successful and allowed a more satisfactory examination of the patient. As an additional finding it was discovered that the left corneal reflex was abolished. The injection performed on the right side did not ruin the corneal reflex on that side. It was then considered that a diagnosis of left-sided acoustic neurofibroma was correct and surgical exploration of the left cerebellopontine angle was advised. On April 16, 1936, Mr. McConnell operated and found a large acoustic neurofibroma on the left side, and as far as he was able to see the right cerebellopontine angle was intact. The tumour was incised and the core removed by suction. Unfortunately, death from complications occurred 18 days later. Necropsy was performed and the remains of a left-sided acoustic neurofibroma were found. The tumour was quite large and had deeply indented the left side of the pons. More important still was the marked distortion of the brainstem so that the pons and medulla were pushed far to the right of the midline and evidently compression of the right side of the pons against the petrous portion of the temporal bone had taken place.

DISCUSSION

These two clinical cases are reported for two main reasons: firstly, to add to the clinical syndrome of acoustic neurofibroma, and, secondly, in the hope that some light may be thrown on the actual mechanism involved in the production of a certain type of trigeminal pain.

In this first category, argument might arise that the occurrence of this type of pain identical with that of tic douloureux represents a mere coincidence. A moment's reflection would show that this is not so. Both tic douloureux and acoustic neurofibroma are rare diseases and their simultaneous appearance in the course of a pathological process involving the fifth nerve apparatus is beyond the bounds of coincidence. The appearance of pain on the opposite

side to the tumour ceases to be so extraordinary when the necropsy material is considered and it is realized that the pons was not merely compressed on the side of the tumour but damaged in its entirety by the change in its whole normal anatomical relationships. Cases enough have been published of areflexia cornealis and anæsthesia in the domain of the fifth nerve on the opposite side to the tumour to make the more rare appearance of paroxysmal pain, also on the opposite side, not so devoid of explanation. So far as my knowledge is concerned, while cases have been recorded of bilateral objective fifth nerve damage no mention has been made of bilateral paroxysmal pain during the course of acoustic neurofibroma.

The second and more interesting point in these cases is that the pain was identical in all respects with that seen in tic douloureux, a disease wherein the pathological cause is, up to date, entirely unknown. Another disease of very different character, namely, disseminated sclerosis, will at times produce the same pain syndrome and frequently it is bilateral. Two cases [4, 5] have been recorded of this disease with necropsy wherein a sclerotic plaque was found at the root entrance zone of the fifth nerve on the side of the pain. Further it has been observed that in all three diseases—tic douloureux, acoustic neurofibroma, and disseminated sclerosis—the pain is relieved by injection of the peripheral branches of the fifth nerve with alcohol. In one case of disseminated sclerosis reported by me [5] relief was obtained by surgical section of the posterior root. The inference from this is obvious, and that is that the explosion of pain depends entirely on incoming trigger-like stimuli and pain ceases when there is a dead and non-functioning afferent pathway.

The pathological changes found up to date in cases of tic douloureux are either nil or not sufficiently explanatory as to the essential cause of the disease. Harris [6] has suggested very reasonably that septic neuritis of the terminal filaments of the fifth nerve in contact with diseased teeth and sinuses is a prominent factor in the production of the disease. He noted, very early, that the second and third divisions and just the branches more in contact with sepsis are the first to be affected and that first divisional involvement is late or not at all. In cases where the teeth are sound, Harris assumes a previous infection and caries in the milk teeth. Again, this particular pain syndrome is practically confined to the fifth and ninth cranial nerves, the latter in contact continuously with tonsillar sepsis. Harris also invokes heredity and trauma as possible factors.

There are points militating against an unreserved acceptance of the above as the whole explanation of the pain mechanism. Dental, tonsillar, and sinus infections in this day and age are excessively common, and while tic douloureux is rare, glossopharyngeal neuralgia is even more so, in spite of the fact that tonsillar sepsis is almost universal at certain ages. Hereditary influences cannot be invoked since direct transmission of tic douloureux from parent to child is a very rare observation, and to fall back on some special constitutional predisposition is begging the question. Again, it is well known

that nerves may be bathed in pus, as in osteomyelitis of the jawbone or elsewhere, and no neuritis appears, and it has been observed frequently that peripheral nerves are highly resistant to contiguous septic processes. Dental caries in Great Britain is extremely common and much less so in the United States, and yet to my limited observation the incidence of tic douloureux seems about the same. Finally, to assume a septic neuritis as the sole cause of the particular type of pain syndrome under discussion one would wish for more evidence such as numbness, reflex and trophic changes in at least the majority of cases of tic douloureux, as well as the pain which is usually the solitary symptom of the disease.

In two diseases such as acoustic neurofibroma and disseminated sclerosis the gross pathology is known. In tic douloureux there is no manifest pathology. It might be reasonable to assume that all three diseases of very different ætiology must work through a common factor to produce so identical a pain syndrome. Already it has been mentioned that cutting the posterior root of the fifth nerve in disseminated sclerosis stops the pain. Of more interest is the case mentioned by Cairns [7] wherein a case of acoustic neurofibroma with paroxysmal trigeminal pain was operated on and the tumour removed. The pain did not cease, however, and second operation to cut the posterior root was necessary and was then successful. Foerster,[8] to explain such a pain syndrome, suggests a state of functional hyperexcitability in the nerve apparatus caused by many and different influences. All incoming stimuli in such cases are responded to by an explosion of pain. This hyperexcitability may wax and wane with the fluctuations of the disease; its remissions and exacerbations and finally the patient's miseries can be put an end to by blocking all incoming stimuli with alcohol or by surgery. Septic infections along the nerve pathway, trauma, vascular disease, sclerosis of the root entrance zone, tumours contiguous to the nerve root and pressure on the side of the pons may each be the causal factor in any given case, and all work through a common mechanism, namely, creating in some way a state of exaggerated irritability of the ninth and fifth nerve apparatus and for some unknown biological reason largely confined to these two cranial nerves. Once this state is induced it is possible that a conditioned reflex is laid down and facilitation occurs, making it more easy each time for pain to be produced. As an analogy, but occurring in the motor system, one thinks of facial spasm, a functional condition of increased irritability of the seventh cranial nerve. This has an insidious beginning, but once the motor activity appears it spreads to include all the areas supplied by the seventh nerve and is permanent. It has, however, the same fluctuation in degree as tic douloureux and is likewise relieved by blocking the nerve with alcohol. Again, nothing of quite the same nature is seen in the nerves of the trunk or extremities, and as a further analogy in one of Cushing's earlier cases of acoustic neurofibroma a facial spasm appeared, and in one case of my own a similar phenomenon occurred during the growth of the tumour. Facial spasm often makes its

appearance after recovery from a mild Bell's palsy. As the facial muscles recover their power, instead of normal activity, there is overactivity and spasm. A similar situation with the fifth nerve is recorded by Harris.[9] In a group of patients of his and for no obvious reason anæsthesia of the fifth nerve area appeared. Following the spontaneous disappearance of anæsthesia, a tic douloureux syndrome appeared and persisted. While incoming afferent stimuli start a pain in tic douloureux, corresponding efferent impulses exaggerate and intensify facial spasm. Facial spasm may be bilateral, and this is just as rare as bilateral tic douloureux, but a case published by me [10] as paraspasmus facialis was really a bilateral facial spasm. The age-incidence of facial spasm is similar to that of tic douloureux, and in all probability the underlying mechanism of the two diseases is identical and rests in the state of hyperexcitability of a cranial nerve, conditioned and facilitated by one cause or another. At first partial, transient, and separated by intervals of remission, it later involves all the branches of the nerve, and becoming constant in character, it is more and more readily induced by afferent or efferent stimuli.

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THE DIAGNOSIS OF CHRONIC SUBDURAL HÆMATOMA OF TRAUMATIC ORIGIN

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INTRODUCTION

Within recent time there has been a considerable increase of the literature on chronic subdural hæmatoma. The personal observation of several cases recently within the space of a year is evidence of its clinical importance and is perhaps sufficient justification for redrawing attention to this not uncommon condition. Examination of the literature suggests that certain aspects of the symptomatology are not receiving the recognition they deserve; the cases here recorded are important in that they illustrate those aspects to which it is desired to draw attention. Failure to bear in mind the possibility of the condition may result not only in valuable time being lost before the correct treatment is instituted, but may prove fatal to the patient.

No useful purpose is served by distinguishing between the more acute and the more chronic types of subdural hæmatoma. There is, however, a type of case in which severe and sometimes rapidly fatal symptoms of intracranial hæmorrhage develop immediately after trauma. Operation or autopsy shows that the lesion in some of these cases is an acute subdural hæmorrhage. In the author's opinion such cases should not be regarded as examples of chronic subdural hæmatoma. There is sometimes a tendency to confuse these two states; it is felt that case 6 reported by Kaplan is essentially an example of an acute subdural hæmorrhage. In chronic subdural hæmatoma the latent interval which elapses between the occurrence of trauma and the onset of symptoms varies considerably, and in those cases where symptoms develop immediately after trauma the initial lesion is presumably a small subdural hæmorrhage which passes unrecognized as such and gradually develops into a true hæmatoma; in cases where the latent period is long, it seems probable that the slowly leaking blood collects and does not give rise to symptoms until after a definite hæmatoma is formed.

It is proposed in this paper to give a clinical description of the cases observed and to limit subsequent discussion to a consideration of the occurrence of raised intracranial pressure.

CASE REPORTS

Case 1.—M.B., male, age 5 months.

The history is incomplete as the patient had only been adopted by the foster

parents one week previous to the onset of symptoms and had seemed well at that time. As far as could be ascertained the infant had been previously healthy and there was no history of trauma ; details of the birth were unknown.

State on Admission.—The infant was deeply comatose, groaning occasionally and moving all limbs ; there was some vomiting ; the temperature was 100° F. ; meningeal signs were absent. The head was large and there was faint bruising of the skin of the right frontoparietal region ; the fontanelles were tense. The eyes were bulging and there was an external divergent strabismus. There was bilateral ptosis and the pupils were fully dilated and inactive to light. There was marked bilateral papilloedema of the hæmorrhagic type.

The diagnosis made was that of severely raised intracranial pressure from an undetermined cause. In view of the almost moribund state of the patient it was decided not to investigate the condition further and the infant died within a few hours of admission.

Autopsy.—There was faint external bruising of the subcutaneous tissue of the right frontoparietal region, and an effusion of blood into the pericranial tissue of that area and into that of the left parietotemporal region. A subdural hæmatoma of considerable size lay over the convexity of the right cerebral hemisphere, particularly in the parietooccipital region, and a smaller one over the convexity of the left cerebral hemisphere. On both sides the lesion was more marked adjacent to the superior longitudinal sinus. The sites of origin of the hæmorrhage were not determined. There was a considerable degree of internal hydrocephalu present, and the cerebrospinal fluid in the ventricles was free of blood. There was no evidence of any external hydrocephalus. The skull was normal apart from its hydrocephalic shape and abnormal separation of the sutures.

Case 2.—W. T., male, age 40 years.

History.—The patient was well until ten weeks previous to admission to hospital, when he developed a feeling of soreness at the back of the head and pain there on coughing. The pain was at first intermittent, but gradually became more constant and severe, and was associated with slight general headache. He continued to work as an engine driver, but after a period of six weeks developed blurring of vision and diplopia. During the month previous to which he came under personal observation the headaches became easier, but the soreness and pain at the back of the head and neck continued. Apart from vomiting on two occasions there has not been any other symptoms.

State on Admission.—The patient was fully conscious, cooperative, and in no severe pain. There was marked bilateral papilloedema of the hæmorrhagic type. The visual fields were normal apart from some enlargement of the blind spots. The pupils were of medium size, and the left was slightly the larger ; they reacted normally. The ocular movements were normal apart from some limitation of outward movement of the left eye which showed a slight downward and inward strabismus. There was a trace of weakness of the lower part of the left side of the face on voluntary movement. The motor system was normal apart from slight hypotonia of the left upper limb. The reflexes were normal, but on one occasion the tendonjerks of the left upper limb and the left kneejerk were increased. The blood pressure was 140/74. External examination of the skull did not reveal any abnormality. X-ray examination of the skull showed some local thinning of the cranium at the vertex on the right side, with a much enlarged venous marking extending from this point to the base ; the sella turcica was enlarged. The cerebrospinal fluid was clear and colourless and had an initial pressure of 400 mm. of water ; the cells were normal ; the protein content was 0·08 per cent., and there was a trace of globulin present.

The diagnosis made was that of increased intracranial pressure from an extracerebral lesion, probably a meningioma, situated in the right posterior parietal region.

On admission the patient denied a history of trauma but later stated that five days before the onset of symptoms he had received a fist blow of moderate severity in the left temple, without any obvious ill-effect. In view of this history of trauma, it was felt that there was a possibility of the lesion being a subdural hæmatoma. During the month that elapsed whilst the patient was under observation, it was noticed that the retinal hæmorrhages disappeared and the papilloedema largely subsided without the onset of any consecutive atrophy of the discs. During this time the patient was confined to bed and the suggestion was made that the supposed hæmatoma was shrinking; by this time the patient was free of all symptoms. In view of the sparsity of physical signs and the unusual subsidence of the papilloedema, ventriculography was attempted; neither lateral venticle could be located.

Operation.—The right posterior parietal region was explored, and a large encysted subdural hæmatoma was found and evacuated. The patient made an excellent recovery.

Case 3.—C. W., male, age 47 years.

History.—The wife of the patient stated that he was well until six weeks previous to admission to hospital, when he was knocked down by a motor car whilst returning home from work. He sustained a small cut over the right temple and a contused right eye, but was not rendered unconscious. He was taken to the local hospital, and sent home without being detained. He seemed a little dazed on reaching home but slept well that night, and seemed normal on the following morning. During the next three weeks he seemed well and continued work as a builder. He then complained of frontal headaches, which recurred in increasing frequency and severity, and was observed to have trembling of both hands, more marked on the right side. There was slight vomiting, increasing unsteadiness of gait and progressive mental apathy. During the two days previous to coming under personal observation he had been very drowsy and occasionally comatose.

State on Admission.—The patient was in a condition of rousable coma; the pulse was slow (40–50 beats a minute) and there was frequent yawning. There was intense bilateral papilloedema with many old and recent hæmorrhages. The pupils were of medium size, and the left was slightly the larger; both reacted to light. There was doubtful asymmetry and weakness of the lower part of the right side of the face. He could move all limbs, but there was a flaccid weakness on the right side, more marked in the upper limb. The tendonjerks were all present, but less easily elicited on the right side; the plantar responses were extensor; the right abdominal reflexes were absent. Pinprick appeared to be appreciated normally on both sides of the body; other sensory examination was impossible. Blood pressure was 130/70; temperature was normal. There was marked tenderness of the skull to palpation and percussion in the right frontal region. On the few occasions when he could be roused, there appeared to be marked difficulty in naming objects, but in view of the comatose condition of the patient this was not interpreted as evidence of a true dysphasia. The cerebrospinal fluid was clear and colourless, and appeared to be under increased pressure (no measurement recorded); protein content was 0·08 per cent., and there was a trace of globulin present; cells were normal.

The diagnosis made was that of a leftsided subdural hæmatoma, but in view of the marked tenderness of the skull in the right frontal region it was decided to explore both sides.

Operation.—The left prefrontal area was trephined, and no hæmatoma was found. Exploration on the right side revealed a large tense encysted subdural hæmatoma. This was evacuated with as little disturbance as possible and the patient made a complete recovery.

Case 4.—T. R., male, age 82 years.

No history was obtainable of the onset of symptoms.

State on Admission.—The patient was an old man, very collapsed, semiconscious, mumbling incoherently at times and resenting examination; occasionally he would try to get out of bed. There was almost continuous twitching of the left side of the face and of the right upper limb; there was a flaccid paralysis of the left upper limb. The fundi showed, as the only abnormality, some arteriosclerotic changes. Both kneejerks were absent, the anklejerks were present and there were bilateral extensor plantar responses. The blood pressure was 200/90, and there was marked thickening and tortuosity of the peripheral arteries. Meningeal signs were absent. External examination of the skull was normal. There was incontinence of urine and fæces; the temperature varied from 100° F. to 101° F., and the clinical picture remained unaltered until death, two days after admission. The cerebrospinal fluid was clear and colourless; no biochemical or cytological examination was made; the pressure was not raised.

The diagnosis made was that of diffuse cerebral vascular disease; it was assumed that there were multiple thrombotic lesions, and possibly a small rightsided cerebral hæmorrhage in addition.

Autopsy.—There was a large encapsulated subdural hæmatoma covering the greater part of the right temporal and parietal lobes. Apart from flattening and senile shrinkage the underlying brain was normal. There was generalized and severe atheroma of the cerebral arteries. The site of origin of the hæmorrhage was not ascertainable. The skull was normal.

Case 5.—L. S., female, age 43 years.

(This case is recorded because of the unusual operative findings, and because the clinical picture was suggestive of a chronic subdural hæmatoma, which was the preoperative diagnosis. It is not included in the subsequent discussion.)

History.—The patient was well until one week previous to the onset of symptoms when, one night, she got out of bed and pulled the washstand on top of her. A week later she awoke during the night with a severe headache, and vomited; she got out of bed and walked into an adjacent room, on reaching which she apparently fell and struck one side of her head, and as a result of this blow she lost consciousnes. Later in the morning she was found lying semiconscious on the floor, and was eventually taken in that condition to hospital, where she stayed for one month. So far as can be ascertained she remained semiconscious for four days, after which her general condition improved. When she came under personal observation, which was one month after the onset of symptoms, she stated that for one week after her collapse on the floor she had had frequent severe pains in the right side of her head, and had been unable to open the right eye. During this time she had paralysis of the left upper limb, and had complained of a sense of uselessness of the right limbs when the headaches were particularly severe. She also had difficulty in speaking, and fluids dribbled from the right angle of her mouth. On admission she was drowsy and apathetic, on account of which it was difficult to ascertain her symptoms with accuracy. For about three weeks she had had frequently occurring visual hallucinations; whether these occurred only on one side of her field of vision was never ascertained beyond all doubt. They appeared as fully formed figures and objects, such as vague whitish figures approaching her from round a distant corner, a fireplace with people seated round it, brightly coloured headgear worn by imaginary patients, black and white dogs. For about two weeks she had noticed a tendency to fail to see objects on her right side, and she had frequent diplopia.

State on Admission.—The patient was plethoric and obese, drowsy in appearance and facile in manner. There was marked bilateral papilloedema. Bedside examination of the visual fields revealed a left homonymous hemianopic defect with some constriction of the right lateral fields. The pupils were of moderate size and the left was slightly the larger; they reacted normally. There was a slight internal strabismus of

the left eye and diplopia on looking to the left. The lower part of the right side of the face was asymmetrical and weak. The outstretched right upper limb tended to droop a little, and the handgrip was a little less strong on that side. The motor power of the lower limbs was impaired. All tendonjerks were exaggerated, more so on the left side; the abdominal reflexes were absent; the plantar responses were extensor but within a short time of admission they became equally flexor. Sensation was normal apart from slight impairment of the sense of position in the left digits. The blood pressure was 124/70. External examination of the skull revealed as the only abnormality faint bruising of the left periorbital region. X-ray examination of the skull was normal. The cerebrospinal fluid had an initial pressure of 190 mm. water: it was clear and colourless; the cell content was 6 per c.mm.; the protein content was 0·085 per cent., and there was a trace of globulin present.

The diagnosis made was that of a subdural hæmatoma situated in the right temporal region.

Operation.—A right temporal exploration was made. Through the unopened dura mater the brain was observed to be darker and more yellow than normal, and on reflecting the dura it was seen to be unusually vascular. Just above the Sylvian fissure there was a soft area in the brain which on being needled yielded about 10 c.cm. of old blood-stained fluid. Incision into this area revealed a large hæmatoma extending into the temporosphenoidal region. The hæmatoma was evacuated and the patient made an uneventful recovery.

DISCUSSION

It is apparent that there was an increase of the general intracranial pressure in three out of the four cases of subdural hæmatoma here recorded; this increase was most severe in the infantile case and only absent in the senile case. In another instance, not here recorded, that of a boy, age 15 years, who had a large subdural hæmatoma in the left frontotemporal region, for one month there had been persistent headache and vomiting, and here also there was intense papilloedema, indicating a marked increase of the general intracranial pressure. It is of importance to determine why raised intracranial pressure occurs in some but not all cases of chronic subdural hæmatoma, for it would seem that the symptomatology of the condition is determined largely by its presence or absence. Its presence results in a much more definite clinical picture, which may have to be differentiated from other common conditions such as cerebral tumour; in its absence, the clinical features of the condition are vague and difficult of recognition. It is suggested that its occurrence is determined largely by the age of the patient. Little attention appears to have been given to this point by the many authors who have contributed to our knowledge of the condition. The usual practice of considering separately the condition as it occurs during infancy and during adult life is probably partly responsible for this neglect of the age factor; neurologists see all but the infantile cases, which tend to be referred to the pædiatrician. An examination of the condition, as it occurs throughout life, suggests that there is a sequence of symptomatology which at present is not receiving due recognition.

Trotter's account of the probable source of the hæmorrhage and of the causation of symptoms in cerebral compression of this type in part explains

why there may be such variety and variability of the clinical pictures with so few symptoms and signs; the more recent work of Gardner and others offers additional explanation of their late onset and variability. It seems probable, however, that the indefinite clinical picture on which emphasis is usually laid in describing this condition only occurs with any degree of constancy during the later decades of life. The present writer suggests that during these years, and especially in the presence of such conditions as atheroma of the cerebral arteries, chronic alcoholism and dementia, the degree of shrinkage of the brain which is present probably prevents the occurrence of any increase of the general intracranial pressure, with the result that the clinical features of the condition are correspondingly indefinite. It has proved difficult to obtain information concerning the ages at which the normal human brain attains final adult dimensions and at which it normally commences to undergo shrinkage. According to Berry, the former occurs between the eighth and eleventh years of life; it seems not improbable that shrinkage also commences at a correspondingly early age. During the period in which the brain is enlarging and moulding the skull, rapid and severe increase of intracranial pressure is likely to be of frequent occurrence in this condition, with the result that the clinical picture is correspondingly more sharply defined; if the fontanelles are still open, the cranial bones will tend to yield to their fullest extent before the rising pressure. Once shrinkage of the brain has commenced, it is suggested that raised intracranial pressure gradually ceases to occur with such severity and frequency, until in the senile period, where the cerebral volume is minimal, it probably never occurs.

A comprehensive review of the records of cases reported in the literature fully supports the view that the clinical picture of the condition and the occurrence of raised intracranial pressure are both alike determined by the age period in which the lesion develops. During the infantile period, so constant and so marked is the increase of intracranial pressure which occurs that the clinical picture closely simulates that of 'idiopathic' hydrocephalus, as has been emphasized by Peet and Kahn; case 1 is an example. During the remainder of the growing period and during the early and middle periods of adult life, clinical evidence of raised intracranial pressure is commonly present: cases 2 and 3 are examples. Thus papilloedema is of common occurrence at these periods of life, being present in approximately 60–70 per cent. of cases; where it is absent, the frequent occurrence of such a group of symptoms as progressive headache, vomiting, drowsiness and coma indicates the presence of raised intracranial pressure. During senescence, evidence of raised intracranial pressure is very uncommon in this condition and the symptomatology is more constantly vague and difficult of recognition; case 4 is an example.

References in the literature concerning the occurrence of raised intracranial pressure are variable and in some cases, it is felt, in need of amplification. Trotter states that definite optic neuritis is a rarity. Martin remarks

that there is little rise of the general intracranial pressure and that signs of this are usually absent; he says, however, that papillœdema has been recorded quite frequently, especially in the rather acute cases. Brain states that papillœdema is often absent, though with reference to intracranial birth injuries he mentions that papillœdema and retinal hæmorrhages may be present and the fontanelles bulging and non-pulsating. Grinker refers to the paper by Peet and Kahn in connexion with the condition in infants; in discussing the adult form he states that very slowly signs of increased intracranial pressure develop, such as headache, choked disc, slow pulse and, often, vomiting. Osler and McCrae mention that papillœdema is unusual. Critchley, in a recent review, writes that symptoms directly referable to the hæmatoma are vague and usually most difficult to evaluate, that mental changes are the most characteristic symptoms and are very rarely absent, and that papillœdema is sometimes found. Munro, in a review of 62 cases, reports changes in the fundi (presumably papillœdema) 10 times, and in the 21 cases in which the blood pressure was raised this was attributed to the increased intracranial pressure which was present; unfortunately he only gives details of a few cases and it is difficult to accept all of these as examples of the condition under review. In a recent paper in which he reports and discusses the symptomatology of 16 cases, Furlow writes that headache is the most common complaint and choked disc the most common finding. The author is in agreement with this statement, though it is difficult to agree with him that the symptomatology of the condition is vague, for in all but the elderly and senile it tends to be one of raised intracranial pressure, most characteristically so during the infantile period.

Note on Case 5.—Cases of traumatic intracerebral hæmorrhage of this type are uncommon. Oppenheim mentions that trephining for a traumatic hæmatoma of the dura mater has frequently been without result because the hæmorrhage has had its site, not in the meninges, but deep in the substance of the brain. Moulonguet refers to a few similar cases reported in the literature. Craig and Adson have recently described nine cases of spontaneous intracerebral hæmorrhage, in some of which trauma or strenuous exercise were contributing factors.

SUMMARY AND CONCLUSIONS

1. Four cases of chronic subdural hæmatoma and one case of intracerebral hæmatoma of traumatic origin are described.

2. The frequency of the occurrence of raised intracranial pressure in chronic subdural hæmatoma is stressed and discussed.

3. Emphasis is laid upon the relationship which appears to exist between the age of the patient and the occurrence of raised intracranial pressure in this condition.

4. The earlier in life the subdural hæmatoma develops, the more frequent and severe does the raised intracranial pressure tend to become.

5. It is only during the later years of life, when raised intracranial pressure is uncommon in this condition, that the clinical picture is so constantly vague.

The author gratefully expresses his thanks to the following members of the Honorary Staff of the Birmingham General Hospital for permission to refer to their cases : Dr. Stanley Barnes, Professor Leonard Parsons, Professor K. D. Wilkinson, Professor Haswell Wilson and Mr. F. A. R. Stammers.

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Editorial

A GAP IN NEUROPSYCHIATRIC KNOWLEDGE

THE rivalry and antagonism between Neurology and Psychiatry are happily passing away, and it has been part of the mission of this JOURNAL in welcoming both subjects within its purview, to assist in their rapprochement. Most of those who are interested in these two subjects would adhere to Huxley's dictum, 'No psychosis without a neurosis,' and therefore it behoves every psychiatrist, when describing the vagaries of his patients, to give a thought to what is going on in the brain, and every neurologist to ponder what variation of cerebral function—temporary and reversible as it may be—may underlie the delusion, the manic excitement, the anxiety or the hysterical fugue of the psychotic or psychoneurotic patient.

Knowledge of how the brain works is increasing rapidly and older conceptions of localization of function are being revised and corrected. It is being realized more and more that in many respects the brain works as a whole, yet that certain areas, possessing certain cytoarchitectural structure and arrangement, have the duty of organizing and controlling special functions. As Kuntz remarks in comparing the cortex of man with that of animals: 'As the cortex increases in expanse it also undergoes regional differentiation, with the result that more and more cortical areas can be mapped out on the basis of structural differences. These structural differences are not without functional significance; consequently new cortical areas may in a very real sense be regarded as new cortical organs.'

Nor is it only in the cortex that new knowledge of functional localization is being obtained. In that crowded area the

diencephalon and mesencephalon considerable exactitude is beginning to emerge. We know that centres in the diencephalon regulate and control autonomic activity, while those in the mesencephalon are intimately concerned with tonic variations in skeletal musculature. It is established that nuclei in the diencephalon control the muscles of the eye, the contraction of the bladder and uterus, the tonic contraction of blood-vessels, regulate body temperature, secretory activity of salivary, lachrymal, sweat, sebaceous and other glands, govern carbohydrate and protein metabolism, elimination of water and the trophic regulation of the skin and subcutaneous fatty tissue. But in the same area are centres which play an important rôle in the affective life of the organism. It has been shown that in animals normal expressions of fear and rage depend on the integrity of the diencephalon. This area, moreover, is concerned not only in automatic activity but takes a hand in the regulation of skeletal muscle control. We may laugh voluntarily (cortical) or involuntarily (thalamic), and to some extent we can control involuntary laughter if the stimulus is not too strong or too ' relevant,' though we cannot control the acceleration of our hearts or respiration or our carbohydrate metabolism.

In the realm of Psychiatry we are dealing primarily with distorted and confused affective impulses which no doubt secondarily give rise to distorted ideas and distorted behaviour. It is now generally admitted that however involved is the delusional system of the paranoiac, however grotesque the behaviour of the manic, the schizophrenic, or the hysteric, the basis of the whole trouble is emotional. At the same time, in our studies both of the psychoses and psychoneuroses, we constantly meet with physical manifestations of disturbances of diencephalic and mesencephalic centres. The lowered activity of all bodily functions in depression, the intense metabolic and visceral activity of the manic, the ' frozen ' muscle-tone of the catatonic and the baffling and conflicting autonomic activities of the anxiety case all exemplify this. It is clear therefore that diencephalic and mesencephalic disturbance is a dominant factor if we are to interpret these conditions in terms of disturbance of neurological function. In attempting such inter-

pretations it must be recognized that practically all of these symptoms are reversible, that we are therefore dealing with alterations of function and not of structure, and that in consequence we are likely to find a clue not in the diencephalic centres themselves but in inhibitions and releases which are impingeing upon them from above. Moreover, we are investigating behaviour disorders of an essentially cortical nature, and consequently our final quest must be to discover exactly how cortical influences are conveyed to diencephalic centres. Here is a gap in neurological knowledge.

We know that there is a large bundle of fibres, probably both afferent and efferent, connecting the frontal lobe with the thalamus, and that this body also has connections with parietal, occipital, and temporal lobes; but we know little about the exact function of these tracts. We infer that there must be cortical connexions in both directions with the hypothalamus and that these chiefly subserve inhibitory mechanisms, but we know little of their anatomical paths or how they work.

Hunsicker and Spiegel, experimenting on cats, showed that some cortical impulses governing autonomic function travel in close association with pyramidal fibres, but a'though division of these tracts produced alterations of autonomic activity, further division of extrapyramidal tracts produced a further degree of such alteration. This led them to conclude that at least two paths of cortico-autonomic control existed, one pyramidal and the other extrapyramidal. White dismisses our knowledge of cortical representation of the autonomic nervous system thus: 'Attempts to define a clear cut autonomic representation in the cerebral cortex have not been very successful. Fulton and his colleagues have found a certain degree of vasomotor and intestinal localization in the premotor cortex, but much more work remains to be done before any definite facts can be established.' Kennard, Viets and Fulton, describing a case of a removable tumour in the premotor cortex (Brodmann's area 6), pointed out that in addition to the frequently described components of the syndrome of premotor lesions—forced grasping, emotional instability, confusion and slowing of mental activity—vasomotor changes in the affected extremities occur, but have seldom received notice.

In this case temperature and sweating changes were noted, and the authors refer to the old observations of Eulenberg and Landois, who held that irritation of centres near the motor areas for particular limbs produces pallor and coldness, while hyperæmia and increased warmth are probably the result of a loss of the central influence and may be due to disease of the cortex or of the path from it which seems to pass in the posterior limb of the internal capsule. Their conclusions are that while changes in skin temperature and sweating on the side opposite the lesion indicate that representation of the autonomic nervous system exists in the cortex, further analysis is needed of the anatomical position of this vasomotor area. All that Kuntz can say on this subject is: 'The mechanisms through which cortical impulses exert their influence on visceral functions as yet are not fully known. Most of the data available at present support the assumption that the cortical impulses in question are conducted downwards through fibres of cortical origin which terminate mainly in the hypothalamus; consequently, the cortical influence probably is exerted mainly through the diencephalic autonomic centres.'

It is quite clear from all this that there is little exact knowledge of the anatomy and physiology of cortico-autonomic connexions. Further, when we come to the more vague and general subject of the cortical factor in emotional behaviour we find a welter of confusion and contradiction. Since Bianchi described the 'loss of social sense' and 'sentimentality' of his monkeys deprived of their frontal lobes, many authorities have thought that the cortex in general and the frontal lobes in particular exercise a 'restraining influence' on instinctive behaviour and primitive emotional impulses, but we find Brickner attributing the lack of 'emotional restraint' (observed in a patient from whom almost the whole of both frontal lobes had been removed) to a failure in intellectual synthesis and categorically stating that 'There is nothing in A.'s record to indicate the primary participation of the frontal lobes in emotional function.'

It is clear therefore that here is a gap in neurological knowledge which must be filled if a true wedding of neurology and psychiatry is to take place. Such a wedding need not disturb

the field of interest of either of these branches of medicine, but, on the contrary, would curb the too frequent wild flights of fancy of the purely psychical psychiatrist and quicken the equally undesirable dry-as-dust materialism of the structural neurologist.

Abstracts
Neurology

NEUROPATHOLOGY

[45] **Relation of hypothalamico-hypophyseal system to diabetes insipidus.**—C. Fisher, W. R. Ingram and S. W. Ranson. *Arch. of Neurol. and Psychiat.*, 1935, **34**, 124.

With the aid of the Horsley-Clarke stereotaxic instrument, lesions were placed in various parts of the hypothalamus in 40 adult cats. In 10 instances prolonged and permanent polyuria developed, while in two cats transient polyuria was observed. In seven of the cats with permanent polyuria transient diuresis which preceded the onset of the permanent phase occurred. The transient polyuria was followed by an interval during which normal conditions of water exchange prevailed. In six instances the interval between the day of operation and the onset of the permanent polyuria varied from eight to 12 days. This interval has been called the latent period.

The transient polyuria has been found to differ from the permanent polyuria in the following respects. It develops much more rapidly and reaches a peak much sooner than does the permanent polyuria; the polyuria is primary to the polydipsia during the permanent phase, while the intake of fluid usually exceeds the output of urine on the first day of the transient phase; during the transient phase the output of urine and the intake of fluid may reach proportions never observed in the permanent phase.

The polyuria and polydipsia in the 10 diabetic cats lasted from two to nine months and appeared to be permanent. The output of urine and the intake of fluid for the animals with the most severe diabetes insipidus were five or six times greater than the values for the control animals. As the polyuria increased in intensity the specific gravity of the urine became correspondingly lower. Deprivation of water for several days brought about a reduction in the output of urine to a normal level and deprivation of food resulted in a reduction of the output of urine to about one-half the previous level. During the course of the experiments on the deprivation of water, the animals lost considerable fluid and a negative water balance developed, suggesting that the polyuria is primary. Repeated small doses of pitressin injected subcutaneously caused a reduction in the urine output and the fluid intake to normal levels.

Permanent polyuria was found to occur only in the cases in which there was bilateral injury to the supraoptico-hypophyseal system. Such

injury resulted in marked atrophy of the supraoptic nuclei and marked atrophy of the posterior lobe. Unilateral damage to this system did not cause polyuria, nor did lesions in any of the other parts of the hypothalamus. The possibility that transient polyuria may be related to irritative lesions of the anterior lobe was discussed.

The evidence from this investigation supports the theory that diabetes insipidus is a hormonal disturbance, caused by a deficiency in the secretion of the antidiuretic principle by the posterior or the intermediate lobe of the pituitary gland. The view is set forth that the supraoptico-hypophyseal system sends secretory impulses to these divisions of the hypophysis and that damage to this system at one of three points, the nucleus, the fibre tract and the pars intermedia and pars neuralis, results in diabetes insipidus.

R. M. S.

[46] **Ruptured cerebral varices.**—L. T. Tureen, S. H. Gray and Paul Wheeler. *Arch. of Neurol. and Psychiat.*, 1935, **34**, 1274.

An analysis of 12 cases of cerebral varix, including the two reported in this paper, showed that they are equally divided between the sexes, six occurring in males and five in females. The sex was not reported in one case. The disease is more common in young persons, eight patients being 25 years or under: two new-born infants, two children and four adults between the ages of 22 and 25. The ages of the remaining four patients ranged from 38 to 50.

Clinically, the presence of cerebral varix was unsuspected in all the cases reported. In one instance the varix gave no clinical symptoms; it was accidentally discovered at autopsy. In the two cases of new-born infants, death was produced by increased intracranial pressure caused by a rapidly expanding varix. Rupture of the varix with fatal hæmorrhage occurred eight times; without fatal hæmorrhage once. Sudden increases in intracerebral pressure preceded fatal rupture four times; twice during eclamptic convulsions and twice during severe physical exertion. In one case in which the initial symptom followed trauma of the head sustained during the war, symptoms of pressure persisted for seven years before death from rupture occurred.

The sites of these vascular lesions were of particular interest. Three occurred in the anomalous ophthalmomeningeal vein of Hyrtl, while in a fourth case there was congenital malformation of the varicosed vein of Galen. In a total of seven cases there was involvement of the vein of Galen or of its tributaries or terminus. The pontine vein was varicosed in one case. There was only one instance of involvement of cortical veins.

Cellular infiltration of the wall of the vein was present in three cases. Amsler reported lymphocytic reactions in one case, while in both the present cases a similar invasion of the wall of the vein was observed. The authors do

not believe that the cellular reaction is evidence of a primary inflammatory process or that inflammation is productive of varices. In their studies the most striking picture was that of sclerosis of the vein. Connective-tissue replaced in varying degrees the muscle and elastic tissue elements of the venous wall; the internal elastic membrane, when it was not completely destroyed, was split into lamellæ, and the intima in its thickening and hyalinization resembled closely that of an arteriosclerotic vessel. Probably the cellular reaction was a result rather than the cause of the degenerative process. In 11 of the cases in which analysis was made no evidences of inflammation were observed.

Congenital defects in the wall of the vein are probably the most important ætiological factor in the production of cerebral varix.

R. M. S.

[47] **Cerebrospinal fluid in cases of tumours of the brain.**—H. H. Merritt. *Arch. of Neurol. and Psychiat.*, 1935, **34**, 1175.

The cerebrospinal fluid pressure is usually increased in cases of tumour of the brain. In this series of 182 cases normal pressures were common in cases of tumour of the brainstem or of the pituitary fossa and in those of glioma of a cerebral hemisphere with areas of cystic degeneration. Tumours located on the convexity of the hemisphere, especially meningiomas, may be accompanied by normal or only slightly elevated pressure, since such tumours do not interfere greatly with the circulation of the cerebrospinal fluid.

The cerebrospinal fluid was xanthochromic in 28 per cent. of the cases. Xanthochromia was usually associated with a high protein content. In a few cases the xanthochromia was due to destruction of red blood cells which had been extravasated by the tumour.

The cell count was usually normal in the lumbar cerebrospinal fluid. In 29 per cent. of the cases there were more than six cells, and in only 17 per cent. more than 10 cells, per cubic millimetre. Pleocytosis in the cerebrospinal fluid was due in most cases to an aseptic meningeal reaction to necrosis of brain or tumour tissue near the ventricles. Most reported instances of marked pleocytosis in the cerebrospinal fluid have been cases of tumour of the frontal lobes involving the corpus callosum. Marked pleocytosis is occasionally found in cases of tumour in the region of the pituitary fossa. The pleocytosis in these cases is probably due to localized meningitis resulting from erosion of the nasal sinuses by the tumour.

The protein content of the lumbar fluid was elevated in cases in which the ventricular walls had been involved by the tumour and in cases of tumour in the posterior fossa. The increased protein content of the lumbar fluid in cases of tumour of the brain is apparently due to exudation from vessels in the tumour, and in those of tumour in the posterior fossa, to stagnation of the fluid in the lumbar sac. In cases of supratentorial tumour

increased protein content was almost always observed when the tumour was in the corpus callosum or third ventricle. In cases of neuroma of the acoustic nerve an increased protein content of the lumbar fluid was almost constantly found, which was usually much higher than that of the fluid in cases of glioma of the cerebellum or fourth ventricle. It is probable that in cases of neurofibroma protein is more likely to be exuded into the fluid than in cases of cerebellar glioma.

The determination of the protein content of the fluid of the lateral ventricles and a comparison of the results with the protein content of the lumbar fluid are frequently invaluable in the localization of the tumour. In many cases the information thus obtained will obviate the necessity of a ventriculogram. This is especially true when the protein content of the lumbar fluid is increased.

In order to prevent the admixture of the fluid from the two lateral ventricles, the fluid should be withdrawn from the ventricles at the same time. Correction must be made for blood in the ventricular fluid. It is not necessary for lumbar puncture to be performed at the same time as the ventricular punctures. A satisfactory comparison can usually be obtained if the lumbar puncture is performed within from 24 to 72 hours before the ventricular punctures. Analysis of the protein content of the lumbar fluid or the ventricular fluid is of no value after the injection of air, since this is followed by aseptic meningitis.

The following conclusions derived from the findings may be summarized: (1) When the protein content of the lumbar fluid is high and that of the fluid of both lateral ventricles is normal, the tumour is in the posterior fossa. The increased protein content of the lumbar fluid is due to exudation from the tumour in the posterior fossa and to stagnation of the fluid in the lumbar sac. (2) When the protein content of the fluid from the lumbar region and of that from both lateral ventricles is high, the tumour is in the third ventricle or the corpus callosum, or there are multiple (usually metastatic) tumours. (3) When the protein content of the fluid from the lumbar region and that of the fluid from one lateral ventricle is high, and that of the fluid from the other lateral ventricle is normal, the tumour is on the side in which the ventricular fluid shows the increased protein content, and the tumour extends deeply enough in the hemisphere to involve the ventricular wall.

R. M. S.

[48] **Possible relation of lead intoxication to multiple sclerosis.**—Benjamin Boshes. *Arch. of Neurol. and Psychiat.*, 1935, **34**, 994.

Specimens of cerebrospinal fluid from 28 patients were analysed for lead by the Fairhall hexa-nitrite method.

In one of 16 cases of multiple sclerosis the fluid showed a positive result. The patient had been given sodium iodide, and the urine also showed lead.

Of 12 other cases of various conditions, in only one, a case of lead intoxication, were abundant crystals found in the cerebrospinal fluid. In this case there was 0·2 mg. of lead per litre of urine.

Taking all three studies into consideration, there is no adequate proof for, and ample evidence against, the theory that lead is an ætiological agent in cases of multiple sclerosis.

R. M. S.

SENSORIMOTOR NEUROLOGY

[49] **Spontaneous pain and other subjective sensory disturbances.**—C. Davison and W. Schick. *Arch. of Neurol. and Psychiat.*, 1935. **34**, 1204.

In this presentation an attempt has been made to show that 'central pain' and other subjective sensory disturbances occur not only in cases of pure thalamic lesions, but also in cases of peripheral, spinal cord, bulbar and cerebral lesions.

In the authors' case of lesion of a cranial nerve the subjective sensory disturbances consisted essentially of a burning sensation along the distribution of the trigeminal nerve. The neurofibroma compressing the nerve was undoubtedly the irritating factor for the production of that type of sensation.

In the four cases of lesions of the spinal cord, in addition to 'central pain' there were other subjective sensory disturbances such as burning, 'vibratory electric-like sensations' and distorted thermal sensations, e.g. cold being called hot. In most of the cases superficial sensation was impaired below the level of the lesion. The pain and temperature dysæsthesias were associated with impairment of those forms of sensation. Histological examination showed that the spinothalamic tracts were implicated. In the first case there was also slight involvement of the posterior columns in the region of the cervical enlargement. As in some of Holmes' cases, vibratory stimuli produced painful sensations. That a lesion of the posterior columns might produce 'central pain' is a remote but unlikely possibility.

The thalamus, lesions of which give the classic picture of 'central pain' and other forms of subjective sensory disturbances, was implicated in four cases. Superficial sensation (pain, touch and temperature) was impaired in most of these cases. This, best demonstrated in the first case, is of significance, as in most of the cases recorded in the literature there was more impairment of the deeper than of the superficial forms of sensibility. In the authors' first case a small vascular lesion was confined to the posterior part of the external nucleus of the thalamus along its inferolateral surface. In the other three cases the thalamic involvement was due to compression by neoplasm

and an aneurysm. In one case the left side of the pulvinar was invaded by the neoplasm. The involvement of the parietal portion of the cortex in three cases leaves open the question whether the subjective sensory disturbances may not have been of cortical origin.

Of greatest interest are two cases in which subjective sensory disturbances, consisting of spontaneous pains and ' feelings like electricity ' associated with impairment of the superficial and deep modalities of sensation, were of cortical origin. In both of these cases there was destruction of the post-central and superior parietal convolutions and the thalamic nuclei were completely spared. From these two cases and the few previously recorded by Mills and others it can be concluded that the cerebral cortex is concerned not only with sensory discrimination, but also with appreciation of the more primitive types of sensation, disturbances of which are associated with some of the phenomena previously mentioned.

Davison and Schick consider that they have submitted data which tend to indicate that spontaneous pain and hyperpathia are associated in most cases with incomplete lesions of the spinothalamic tract or its components. Irritation or incomplete destruction of the spinothalamic sensory system may give any one or a group of the phenomena discussed in this presentation.

R. M. S.

[50] **Subdural traction and post-traumatic headache.**—W. Penfield and N. C. Norcross. *Arch. of Neurol. and Psychiat.*, 1936, **36**, 75.

In order to analyse the anatomical basis of intracranial pain the authors studied the observations of 33 intelligent patients during operation with local anæsthesia. Stated briefly, it was found that the dural sinuses are sensitive to pressure, traction, heat and electrical stimulation. The middle meningeal artery and its larger dural branches are also usually sensitive. Cerebral vessels are insensitive, except occasionally for a tributary vein just before it enters a dural sinus or a vessel low in the fissure of Sylvius. The skull, the dura itself, and save in the temporal and frontal lobe, the brain are quite insensitive to cutting or electrical stimulation. The only type of sensation which can be produced from within the cranial cavity is interpreted by the subject as pain or pressure. He usually calls it headache, sharp pain or pressing pain. Pain due to stimulation of the meningeal arteries is well localized to the region stimulated and is often sharp. Pain derived from the dural sinuses is usually referred to a point some distance from the site of stimulation.

The best evidence for the belief that post-traumatic headache is situated in the subdural space is provided by the fact that introduction of air into the subdural space over the hemispheres cures post-traumatic headache in a

high percentage of cases. Under normal circumstances the subdural space contains a small body of fluid quite separate from the cerebrospinal fluid and because of this fluid bed the small movements which occur between the brain and the skull when the head is moved quickly are made possible. The pathological basis of true post-traumatic meningeal headache consists in an intimate adhesion of the arachnoidea to the dura, which causes obliteration of the subdural space in a smaller or larger area. This does not mean dense adhesions such as those of a scar. The sensitive area which is likely to be affected by this adhesion is usually a meningeal artery in the dura or, less frequently, a dural sinus. The chronic pain is due to pressure or traction on one of those sensitive areas because of the rotation in position of the brain produced by the blow and maintained by the adhesion.

Effective therapy must provide for collapse of the ventricular system and the simultaneous introduction of air into the subdural space. As the head is oscillated, the brain, which is shrunken because of the collapse of the ventricles, pulls away from the overlying dural covering with considerable traction due to its own weight. This separation accounts for the cure which results from proper insufflation of air. Failure may occur when this reopening is incomplete, and adhesion continues to stimulate a sensitive area of dura.

R. M. S.

[51] **Primary degeneration of the corpus callosum (Marchiafava's disease).**—L. S. King and M. C. Meehan. *Arch. of Neurol. and Psychiat.*, 1936, **36**, 547.

First described in 1903 by Marchiafava and Bignami, primary degeneration of the corpus callosum has been reported in about 40 males—all Italians. It is characterized by demyelinization of nerve-fibres, with relative retention of axiscylinders: the lesions occur invariably in the corpus callosum, but sometimes in other parts of the brain as well.

In the symptomatology psychic disorders are frequent and often are severe enough to require treatment in a mental hospital. The most constant somatic finding is convulsions of an apoplectiform or epileptiform type. Tremors, dysarthria, transitory hemiparesis, paresis of the legs and variable reflex changes have been observed in different patients. Sensory disturbances, except headaches, have not been reported. Autonomic disorder may be present in the form of impotence or incontinence. Bignami and Nazari emphasized the severe disorders of nutrition in the terminal stages.

The course is variable, from three to six years, and usually commences in middle age; remissions may occur and the early psychic symptoms are easily confused with those of alcoholic intoxication.

The pathological changes are distinctive. Nothing on the surface of the

brain gives any hint of the changes seen on section. When the cerebrum is cut the anterior portion of the corpus callosum is seen to be rather sharply divided into three laminæ, of which the dorsal and ventral are normal in colour and consistency, while the middle is softer and pinkish or greyish in colour. This condition of the middle layer is sometimes present throughout the corpus callosum. In many cases, in the posterior parts of the corpus callosum the abnormal area disappears in the region of the midline, leaving symmetrical lesions on the two sides, extending backwards for varying distances. The abnormal area usually stops abruptly at or near the lateral margins of the corpus callosum. The soft, pinkish lamina ordinarily occupies about two-thirds of the dorsoventral extent of the corpus callosum.

As regards ætiology, whenever the clinical history has been obtained it has been noted that the patient was a heavy drinker, either of wine or of wine and distilled liquor.

R. M. S.

Psychopathology

[52] **Symptoms preceding suicide.**—S. J. Minogue. *Med. Jour. of Australia*, 1936, **2**, 598.

A clinical review of the 4,688 known cases of suicide in New South Wales from 1913 to 1929 inclusive reveals that in the great majority of the cases the actual suicide was preceded by a period of insomnia. In some persons this symptom had lasted for many years, in others only a day or two. The causes of the insomnia were very varied, but in the main fell into five well-marked categories: (1) 'Idiopathic'—present for many years and without known causation. (2) Due to physical illnesses—the more prolonged and painful the illness, the graver the risk of suicide. The frequency of suicide after head injuries was surprising. Patients with phthisis, contrary to all medical impressions, comprised more than 1 per cent. The 50 puerperal women in the series point to the fact that on no account should insomnia during the puerperium be lightly treated. (3) A large group with psychological worries. (4) Those with mental disease were common: those with melancholia being much the most numerous. (5) Roughly, about one-third were alcoholics. The frequency of suicide among cases of delirium tremens was an unexpected discovery of the investigation.

The insomnia, therefore, can only be regarded as a symptom of some physical or psychological disease-process. Whatever its cause it led to rapid mental and physical exhaustion. Headaches were usual. Large numbers became desperate, regarded the strain as too great and sought self-destruction as the inevitable ending. The clinical material investigated emphasizes the axiom that it is imperative to treat not only the insomnia, but the patient as well.

C. S. R.

Reviews and Notices of Books

The Essentials of Psychopathology. By G. W. Henry. London: Baillière, Tindall and Cox. 1936. Pp. 320. Price 18s.

THE aim of the writer of this book has been to present to his readers, chiefly perhaps to students and members of the profession, an account of the nature and causes of personality disorders. What might be termed the anatomy and physiology of personality are first discussed; that is to say, its relation to constitution is examined, and the effects on its working of heredity and environment. Therefore the author is concerned with the debatable ground, the no-man's-land (or should we say every-man's-land?) of the marches between the physiological and the psychological. Mental mechanisms, current methods of examination and some clinical syndromes are discussed in a later section. In his studies the author has sought to follow objective lines, is temperate in his conclusions, and has produced a volume which will not alienate the neurologist by its neglect of the nervous system or disappoint the psychopathologist by under-emphasis of the side of the subject that appeals to him.

An Introduction to Psychological Medicine. By R. G. Gordon, N. G. Harris and J. R. Rees. London: Oxford University Press, Humphrey Milford. 1936. Pp. 386. Price 10s. 6d.

As stated in their preface, the intention of the joint authors of this 'Introduction' has been to give the student 'some picture of the structure and function of the normal mind, the nature of psychopathological processes, and the form taken by clinical entities which can be recognized and classified as the various forms of mental illness.' They feel that in his medical curriculum the student should proceed from neurophysiology to psychology 'logically,' then to psychopathology, and finally to the clinical side of the psychoneuroses, psychoses, and mental deficiency. Such a scheme is sound and desirable; it would remove reproaches and at the same time put the whole subject of mental illness in its real setting among the other subjects of clinical medicine, not divorce it as at present, or 'damn' it by faint interest.

Having this end in view, the writers have done well in their task by arranging the book on corresponding lines, although they begin, naturally enough perhaps, where neurophysiology leaves off, without handling much of the latter. Numerous clinical illustrations are provided in the pages of a

readable work, which shows less signs of being a compilation by different authors than most books of the character. The interpretation of not a few of the clinical cases here quoted leans strongly to the psychopathological side; for instance, occupation neuroses are regarded as significant of 'discontent' and as providing 'means of escape,' and the like; but it would not be difficult to show that some of their phenomena cannot be explained by such conventional views.

Theory and Practice of Psychiatry. By William S. Sadler. London: Henry Kimpton. 1936. Pp. 1231. Price 42s.

A VOLUME of well over a thousand pages, covering every aspect of psychiatry, represents a task of considerable magnitude, the accomplishing of which is matter for congratulation. Dr. Sadler's volume is framed on more or less conventional lines, being perhaps all the better for that; its setting out is logical and its consecutive arrangement suitable for purposes of reference. A very large number of clinical cases, sometimes described in rather a profuse manner, swell the dimensions of the book to no little extent. Particular attention is given to 'the neuroses' (about 250 pages), but here the classification adopted leaves much to be desired. They are subdivided into (*a*) psychasthenic states, (*b*) neurasthenic states, (*c*) the hysterias, and (*d*) allied functional nervous disorders. The last of these is a kind of caput mortuum, which comprises 'vasomotor ataxias,' 'motor ataxias,' 'sympathetic irritability,' 'migraine,' and 'constitutional psychoneurotic inferiority.' Such a scheme will hardly satisfy the critical and is open to several objections. Under 'motor ataxia' are included 'tremors and convulsive movements,' the relation of which to neurosis sensu strictiori is nebulous. In this last division (*d*) case-reports again fill the pages, but of inferences and syntheses therefrom little indeed appears. The conception of vagotonia and sympathicotonia, briefly discussed but illustrated by still more clinical cases, has probably been over-simplified and stands in need of revision.

With judicious pruning this book might be lightened at once of some of both its physical and its mental heaviness.

Les Maladies Nerveuses. By A. Van Gehuchten. Fourth edition, revised by P. Van Gehuchten. Louvain: Librairie Universitaire. 1936. Pp. 718.

THE new fourth edition of the textbook of nervous diseases written by the late Professor A. Van Gehuchten, as revised and amplified by his son, shows considerable improvement on its predecessor (1926). Composed in an easy 'lecturing' style and well arranged, the material is divided into the two categories of 'organic' and 'functional.' Good descriptions, well illustrated,

are provided of the 'organic' diseases of the nervous system, and extend over 600 pages; to 'functional' conditions are allotted no more than 50. We do not know that there is much to cavil at in this considerable disproportion; many descriptions of neurotic states furnished by contemporaries would gain in point if they were brief, and less encumbered with verbiage. For its purpose, that of a textbook for students in neurology, the volume is excellently suited, and in this new edition sure to be appreciated. A number of the illustrations lack explanatory legends below them—an omission that might be corrected with advantage.

A Preface to Nervous Disease. By Stanley Cobb. London: Baillière, Tindall and Cox. 1936. Pp. 170. Price 13s. 6d.

Dr. Stanley Cobb's slender book deals in a simple, clear, and yet erudite fashion with a variety of topics that concern the student of the nervous system. Subjects with which his name is associated here find, naturally enough, a prominent place; for instance, the cerebral circulation, the peripheral nerves and neuritis, motor integration and locomotion. These are among the longest chapters, whereas but a few pages are given to each of some others—for example, cerebrospinal fluid, paths of infection to the nervous system. The truth is, we think, that the book will be most enjoyed by those who are already familiar with its subject-matter, for it is rather discursive for the mere beginner and not 'ingoing' enough for such as seek to pursue any one of its themes. In other words, it is less a 'Preface' than a selection by a richly stored mind of neuropsychiatric questions and problems on which there is much to be said by so competent a writer. The book can be picked up and perused at random with interest and profit.

Aphasia: A Clinical and Psychological Study. By Theodore Weisenburg and Katharine E. McBride. New York: The Commonwealth Fund; London: Oxford University Press, Humphrey Milford. 1936. Pp. 634. Price 21s.

The late Dr. Theodore Weisenburg, whose loss all neurologists deplore, spent the last years of his life in pursuing with enthusiasm and concentrated attention the large and difficult subject of aphasia, of which he was known to have long been a student. His labours are enshrined in this packed volume, which easily holds its own with some well-known monographs that have preceded it. Rather less than one-third of the work is taken up with case-reports and methods of investigation, the remainder being devoted to aspects of the problem that concern neurologist and psychologist alike. Broadly conceived, the lines here followed lead to the conclusion that the chief clinical types are the 'predominantly' expressive, receptive, expressive-receptive and amnesic

varieties; that apraxia and agnosia, while closely related phenomena, do not appear as such (definitions are provided to explain the authors' use of the terms) in the 'clear-cut cases of aphasia' here discussed; and that 'pure' forms of limited extent, or cases exemplifying 'the subordinate classes such as the transcortical aphasias or conduction aphasia,' have not been encountered in the authors' series of 60.

It would be impossible in a short review to enter into various criticisms that suggest themselves, and we are content to recommend the monograph cordially to all those who find in its subject-matter a question of unceasing interest.

The Cerebrospinal Fluid and its Relation to the Blood. By S. Katzenelbogen. Baltimore: The Johns Hopkins Press; London: Humphrey Milford. 1936. Pp. 468. Price 22s. 6d.

This is a finely conceived and executed work. Aware of numerous contradictions, of theories as much accepted as denied, of data reliable and unreliable, of conclusions tenable and untenable, that crowd the literature of the cerebrospinal fluid and its relation to the blood, Dr. Katzenelbogen undertook to approach the whole question de novo and to determine for himself, so far as possible, what is established and will remain, as well as what is not. Accordingly, he presents his readers with a complete mise-au-point of his subject. His book is neither a textbook of the fluid nor a laboratory guide, but rather a work of reference in which the knowledge of to-day is sifted, weighed, and judged, in each of its aspects; thus three chapters describe the fluid as such, its formation and circulation, and several more are concerned with its physicochemical composition. Full attention is engaged with problems of the 'barrier' between blood and fluid and its permeability. Every chapter closes with a summary.

It is a welcome addition to the literature of the cerebrospinal fluid and has qualities that make it indispensable to all workers in the field and all who require to familiarize themselves with what has been determined in regard to the fluid and its bearing on clinical neurology. The bibliography covers over 40 pages.

Physiopathologie du Système Nerveux. By Paul Cossa. Paris: Masson et Cie. 1936. Pp. 690. Price 75 fr.

Dr. Cossa's compendium of nervous physiology and physiopathology covers more than its title indicates and is calculated to appeal to the clinician who is not content with mere observation, but wishes to understand the meaning of symptoms and signs. It is remarkably comprehensive, and somewhat of a novelty, we imagine, for the French school. French neurologists have been

reproached with following the clinicoanatomical method to its sterile end; aware of this, a pregnant phrase from Dr. Clovis Vincent's preface shows how he regards the matter: 'Si l'anatomie et la clinique sont à la base de la pratique, la physiologie est à la base du progrès.' Here then is offered to the student a nervous semeiology in which the underlying physiology of symptoms and signs is explained in clear language, aided by a wealth of diagrams, the great majority of which appear to be original. The more we have examined it the more convinced we are of the excellence of the production, whose value is enhanced by that rarity among French books—an index.

Pathology of the Nervous System. By J. Henry Briggart. With 204 illustrations. Edinburgh: E. and S. Livingstone. 1936. Pp. 336. Price 15s.

THERE are not too many compact and well-planned textbooks of neuropathology on the market to-day for this new arrival to fail to find a place. A general account of the processes and reactions of disease in neural tissues is followed by a description of a number of nervous affections from the standpoint of their pathology. So far as these descriptions take the reader they are succinct and accurate, controversial matters being eschewed and only essentials examined. Doubtless, owing to its very qualities of brevity and condensation, the work leaves on the mind the impression of being rather unequal; there is much more variety and complexity in regard to 'birth injuries' than the two pages devoted to that topic convey; on the other hand, although the paragraphs on Huntington's chorea hardly occupy more than half a page they embody the thoroughly sound contention that since the morbid process is diffuse any attempt at clinicopathological correlation is 'difficult'—we might add 'precarious.'

Vitamins and other Dietary Essentials. By W. R. Aykroyd. Second edition. London: William Heinemann (Medical Books). 1936. Pp. 226. Price 7s. 6d.

THE student of the nervous system has to-day to familiarize himself with much more in medicine than seemed to be the case at the beginning of the century, for advances in knowledge in spheres at first glance rather remote have thrown a flood of light on disease-conditions once supposed to be his preserve. This is true in particular of the vitaminoses, so-called; among them are numbered beriberi, pellagra and perhaps subacute combined degeneration—at least, several nervous conditions have definitely a vitamin side, so to say. Dr. Aykroyd's discussion of vitamins is fascinating, no less because of the intrinsic interest of the subject than owing to his animated and often amusing style, coupled with a facility in illustration that is to be envied. He

has written a book more entertaining than an armful of novels and yet pervaded with a sound scientific atmosphere of criticism and suspended judgment.

Exophthalmic Goitre and its Medical Treatment. By O. Israel Bram. Second edition. St. Louis: C. V. Mosby Co. 1936. Pp. 456. Price $6.

A COMPLETE revision of a previous edition (1920) has enabled Dr. Bram to incorporate in his book various increments to knowledge of a still mysterious disease that have accrued in the last decade or more. Its theme is centred on the belief, held with conviction, that exophthalmic goitre can be treated by medical, hygienic, and psychotherapeutic measures more successfully than in any other way. His argument is that the malady cannot possibly be thyrogenous alone, and that the surgeon acts as though he were dealing with a mere local thyroid disease. Operative treatment can therefore at most be purely palliative. We need not follow the argument farther, based as it is on the author's experience of twenty years; everything that can be said and done from a non-surgical standpoint is here weighed, documented, and put forward as a practical contribution to treatment.